AN EPIDEMIOLOGICAL STUDY OF RESPIRATORY DISEASE AND THE HOME ENVIRONMENT IN SEVEN-YEAR-OLD CHILDREN

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DECLARATION BY THE CANDIDATE

I declare that this thesis has been composed by myself specially for the MD degree, and has not been submitted in this form for any other degree or diploma examination. Published papers relating to the material presented are listed in section 1.4.

The work upon which the thesis is based was performed entirely under my direction, although advice and technical assistance were obtained from the Building Research Establishment, East Kilbride, and the Addiction Research Unit, Institute of Psychiatry, London. Their contributions are described in more detail in section 1.3.

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ABSTRACT

AN EPIDEMIOLOGICAL STUDY OF RESPIRATORY DISEASE AND THE HOME ENVIRONMENT IN SEVEN-YEAR-OLD CHILDREN

A cross-sectional study of seven-year-old children was conducted to explore the relationship between damp, mouldy housing and childhood asthma, and the effects of passive tobacco smoke exposure upon respiratory symptoms, lung function and middle ear effusion.

A random cluster sample of 1095 school children were contacted. Following a postal questionnaire to parents, 892 children were examined. Baseline spirometry, exercise-induced bronchospasm (EIB), and impedance tympanograms were measured. Salivary cotinine concentration was determined for 770 children. Bedroom temperature and relative humidity were monitored continuously for 7 days in the homes of 317 children. The repeatability of each of the measurements was assessed.

Among 1000 children with questionnaire data, 123 (12.3%) were reported to have wheezed in the previous year. Recent wheeze was strongly associated with report of mould in the home (odds ratio 3.70, 95%CI 2.22-6.15, X^2 27.7, 1df), and this association was substantially independent of other aspects of the home environment. However, reported dampness and mould growth were only weakly associated with EIB and impaired baseline spirometry. Differences in adjusted weekly mean temperature and relative humidity between the bedrooms of wheezy and non-wheezy children were small and non-significant, although in the expected direction (-0.4 degC, t -1.3, 315df; +1.1% RH, t +1.1, 315df). Tympanometric findings were unrelated to bedroom conditions. At every level of measured EIB, recent wheeze was reported more commonly for children from mouldy homes, and the association between mould and wheeze was substantially independent of EIB.

These findings confirm those of a preliminary study and suggest that the association between damp or mouldy housing and childhood asthma may be principally due to greater awareness of respiratory symptoms by parents who consider their home to be mouldy. Further studies of this association will benefit from objective measurements of both exposure and disease.

Cotinine was detected in the saliva of 85% (658/770) children. Six children had levels greater than 15 ng/ml, which may indicate experimentation with active smoking. Cotinine concentrations were strongly related to the number of smokers in the household, female sex and rented housing. Most respiratory symptoms, including wheeze, were not associated with salivary cotinine. All spirometric indices except FVC were inversely correlated with cotinine level, the effect being greatest for end-expiratory flow rates. Adjusting for sex, height, test conditions and housing tenure, differences in FEF75-85% and FEF75% between the top and bottom quintiles of salivary cotinine were each about 7%, equivalent to a reduction of 1.1% (95%CI 0.1%-2.1%) per doubling of cotinine concentration.

Further cross-sectional studies of passive smoking in childhood should include measures of end-expiratory airflow. The long-term significance of these spirometric changes can only be assessed by longitudinal studies, preferably using biochemical markers of tobacco smoke exposure in subjects who have never actively smoked.

Tympanograms indicating middle ear effusion (Type B) were found in 9.4% (82/872) children. The housing characteristic most strongly related to effusion was the number of smokers in the household, the odds ratio for two or more smokers (compared to none) being 1.9 (95%CI 1.1-3.4, X^2 4.1, 1df). Tympanometric abnormalities were strongly related to salivary cotinine level, the odds ratio for effusion being 1.14 per doubling of the cotinine concentration (95%CI 1.03-1.27, X^2 6.6, 1df). Adjustment for sex, housing tenure and a range of specific housing variables made little difference to this result. At least one-third of middle ear effusions in this population were statistically attributable to passive smoke exposure.

These findings are consistent with three case-control studies and one population survey of this age-group, and suggest that middle ear effusion should be added to the list of hazards attributable to passive smoking.

TABLE OF CONTENTS

4. RESULTS

5. DISCUSSION

8. TABLES

9. FIGURES

10. APPENDICES

1. BACKGROUND

1.1. Preliminary Study

As a vocational trainee in general practice, I conducted a small cross-sectional study of housing conditions and respiratory disease among the seven-year-old children registered with the training practice to which I was attached (1).

The most striking finding was the association between damp or mouldy housing and symptoms of asthma. Among 35 children whose home was reported to be mouldy, 13 (37%) were said to have wheezed in the past two years, compared with 18 (14%) of the 130 children from homes not affected by mould. The associations between damp, mouldy housing and wheeze or nocturnal cough were unlikely to be due to chance ($p < 0.01$) and were independent of housing tenure, parental smoking, gas cooking in the home and family history of wheeze.

However, when the general practice records of the same children were examined for consultations relating to cough or wheeze, the proportion of children presenting with lower respiratory symptoms over the past two years was very similar for mouldy and non-mouldy homes (54% v 53%), and the excess of consultations for wheeze among children from mouldy homes was small and non-significant (17% v 12%). This suggested that the

association between damp, mouldy housing and childhood asthma in the questionnaire data might reflect bias in the reporting of symptoms, rather than a causal relationship. Such bias in the disease information could arise if the threshold for reporting symptoms, or the quality of recall, differed between parents in affected and unaffected homes. Reporting bias in the housing data was also plausible, since the parents of asthmatic children might seek to explain their child's illness and thereby become more aware of potential hazards in the home.

The possibility that there might be bias in the questionnaire information relating to housing conditions and respiratory health implied that further enquiry should attempt to obtain objective measurements of both disease and exposure. The preliminary study had been concentrated in an area of poor quality local authority housing, where dampness was an important local political issue. It was therefore decided that any further survey should attempt a complete population coverage, partly in the hope that reporting bias might be reduced in areas where damp housing had a lower public profile, and partly to allow generalization of the results.

Seven-year-old children were considered a suitable group for further study. They could be readily contacted at school, and were old enough to cooperate with the clinical tests proposed, but were below the age at which active smoking might influence their respiratory health.

1.2. Aims of the Present Study

The principal aim of the study was to investigate the public health importance of damp, mouldy housing as a determinant of both upper and lower respiratory complaints in a representative sample of the seven-year-old population in Edinburgh. This implied adequate evaluation of the role of differential reporting in accounting for any observed association. Objective evidence of relevant disease outcomes and environmental exposures in the home was therefore required.

A subsidiary aim was to obtain biochemical data relating to passive tobacco smoke exposure, and to investigate the relationship between such exposure and both upper and lower respiratory disease.

More specifically, it was proposed that lower respiratory disease should be detected by detailed analysis of the resting spirogram. The degree of

bronchospasm following a physiological exercise challenge would be used as an objective test of asthma. The choice of an objective indicator for upper respiratory disease was less obvious. Measurement of middle ear pressure and effusion by impedance tympanometry was included because the technique is fully objective and recurrent upper respiratory infection is a recognized risk factor for middle ear effusion (serous otitis media or "glue ear"). Parental reports of dampness in the home were validated by monitoring temperature and relative humidity in the child's bedroom. Passive smoke exposure was quantified by analyzing saliva specimens for cotinine, a nicotine metabolite which is a sensitive and specific marker of inhaled tobacco smoke.

1.3. Conduct and Funding

I was personally responsible for the design, execution and statistical analysis of the study, and conducted all the clinical examinations with the assistance of a research nurse.

Monitoring of the home environment was carried out by a non-clinical research assistant working under my supervision. The Department of the Environment Building

Research Establishment, Scottish Laboratory, East Kilbride offered the loan of forty thermohygrographs for the winter 1986-87, and Drs Philip Cornish and Christopher Sanders at the Establishment analyzed the resulting seven-day recordings of temperature and relative humidity using a computer program developed in their department.

Assay of saliva samples for cotinine was performed under subcontract by Drs Martin Jarvis and Colin Feyerabend of the Addiction Research Unit, Institute of Psychiatry, London and Poisons Unit, New Cross Hospital, London.

The principal source of funding for the study was a research grant from the Asthma Research Council. This supported two half-time research assistants, apparatus and running expenses. The research funds provided by my Wellcome Research Training Fellowship were used to cover the cost of collection and frozen storage of saliva specimens and contributed towards their subsequent analysis for cotinine. The cotinine assays were also supported by funds from the Medical Research Council, held by the Addiction Research Unit, Institute of Psychiatry, London.

1.4 Published Papers

The following scientific papers relating to material presented in this thesis have been published, or are in press:

Strachan DP. Damp housing and childhood asthma: validation of reporting of symptoms. Br Med J 1988;297:1223-1226.

Strachan DP, Sanders CH. Damp housing and childhood asthma: respiratory effects of indoor air temperature and relative humidity. J Epidemiol Community Health 1989;43:7-14.

Strachan DP. Repeatability of ventilatory function measurements in a population survey of seven-year-old children. Thorax 1989;44:474-479.

Strachan DP, Jarvis MJ, Feyerabend C. Passive smoking, salivary cotinine concentrations and middle ear effusion in seven-year-old children. Br Med J 1989;298:1549-1552.

Strachan DP, Jarvis MJ, Feyerabend C. The relationship of salivary cotinine to respiratory symptoms, spirometry and exercise-induced bronchospasm in seven-year-old children. Am Rev Respir Dis (in press)

Strachan DP. Impedance tympanometry and the home environment in seven-year-old children. J Otol Laryngol (in press)

2. INTRODUCTORY REVIEW

2.1. Housing and Health

2.1.1. Overview

Historically, the influence of housing on health has been considered of great importance (2) and much of the decline in mortality from infectious disease over the past 150 years may be attributable to improvements in living conditions in the broadest sense (3). In the past twenty years, however, the home environment has received less attention than aspects of individual lifestyle in the fields of medical research and public health policy.

The health hazards of insanitary conditions and gross overcrowding are well recognized, and remain a problem on a massive scale in developing countries. In the United Kingdom, lack of amenities and overcrowded conditions remain a small but significant problem, particularly in "houses of multiple occupation". Along with hypothermia and home accidents, these problems are reasonably well understood, and the ways (if not the means) of solving them are seldom in doubt.

The potential importance of the domestic environment is illustrated by the observation that those in employment spend over half of their time indoors at home (compared to one-quarter of their week at work), and that for

housewives and young children this time may increase to over 20 hours per day (4). Exposure to potential hazards in the home may therefore cumulate to high doses, even though the actual level of exposure is low. The evaluation of low-level risks thereby assumes greater importance, and there is renewed interest in the possibility of incorporating quantitative information on possible health risks into building standards and regulations (5).

A wide range of potential hazards have been comprehensively reviewed within the past three years (4,5). The effects of space and lighting upon health are considered small. Noise, particularly from neighbours, is a common problem, and a direct link to psychological ill-health is difficult to exclude. Existing knowledge is sufficient to recommend standards for sanitation, food storage and waste disposal (5).

Following the decline in "old-fashioned" smoke and sulphur dioxide air pollution in many First World cities, attention came to focus on indoor air quality, which is much less amenable to control by legislation, and presents more complex problems for epidemiological enquiry (4). Air pollution is of greatest relevance to respiratory conditions, but there has been concern that lung cancer incidence may be affected by environmental

tobacco smoke exposure or by radon which accumulates in poorly ventilated dwellings in areas where soils or building materials contain radium. The incidence or severity of coronary heart disease may be influenced by passive smoking or ambient carbon monoxide. Formaldehyde and other volatile organic compounds derived from glues, resins and proprietary cleaning agents are mucous membrane irritants and many are established or suspected mutagens or carcinogens (4-6).

2.1.2. Housing and Respiratory Disease

Both chemical and biological contamination of the indoor air are of relevance to respiratory disease. The possible effects of environmental tobacco smoke have received much attention, and will be discussed later.

Nitrogen dioxide, derived from unvented gas and paraffin appliances, including gas cookers, is toxic to the lung in high doses, causing an acute chemical alveolitis ("silo-filler's disease"). Whether it causes lung damage after chronic exposure to the concentrations found in normal homes is much less clear (4,7). Although the balance of evidence suggests a small adverse effect in children, this effect appears to be outgrown or hidden by other damage to the lung by the age of 10-20. It has been estimated that a study of over 20,000 subjects might be required to have the

power to demonstrate a subtle effect as statistically significant (7).

Other domestic fuels have received less attention in developed countries. In particular, it is remarkable that, with attention concentrated upon outdoor smoke and sulphur dioxide air pollution, there has been relatively little interest in possible effects of open coal fires in the home (8). Wood smoke is a more common exposure in developing countries, where local traditions of construction can lead to excessively high indoor concentrations, as in Papua New Guinea. Although no differences in the prevalence of respiratory abnormalities were found among exposed and unexposed children in that country (9), it has been suggested that chronic exposure to wood smoke may be a cofactor in the development of chronic respiratory disease in middle-aged adults (10).

Recent outbreaks of Legionnaire's disease and the "sick building syndrome" have focused attention upon biological agents in the indoor air. Case-reports of allergic alveolitis and "humidifier fever", an influenza-like illness without pulmonary manifestations, have been linked to contamination of air-conditioning systems with thermophilic fungi. Outbreaks of opportunistic Aspergillus infection among

immunosuppressed hospital patients have been traced to contaminated ventilation systems or building activity (4). These hazards of artificial ventilation and humidification are largely confined to large office buildings and other institutions. In the domestic environment, house dust mites and fungal moulds appear to be the biological agents of most relevance to respiratory disease. These will be discussed further in the next section.

2.2. Dampness and Mould Growth

2.2.1. The Nature of Housing Dampness

No formal definition of dampness in housing has been proposed. An operational definition which might be generally accepted is the presence of visible or palpable moisture on or in the interior fabric of a building. Moisture within a dwelling may arise from water used in the construction process, rising dampness, dampness penetrating through the building fabric, traumatic defects (burst pipes or overflowing tanks) and atmospheric moisture from the biological and domestic activities of the occupants (11).

As much as 1300 litres (300 gallons) of water may be left to dry out of the structure of a newly completed

house. Unassisted, this drying process may take 9-12 months and relies upon the natural ventilation of the building. Dampness is therefore emerging as a problem in small, well draught-proofed "starter" homes which the occupants leave unventilated for much of the week while they are at work (Raw G, personal communication).

Moisture rising by capillary action through the walls of a building should be prevented by a non-porous damp proof course. Houses built before 1920 were not provided with such protection, and defects in the damp proof course of newer houses can occur, either through inappropriate construction, or through soil piled against the outside wall above the level of the damp proof course. Rainwater penetrating through the fabric of the building usually implies a structural defect or fault in the design. Rising dampness (and, to a lesser extent, penetrating dampness) brings with it hygroscopic salts which may absorb moisture from the atmosphere of the room even after the defect is remedied. However, the presence of these salts tends to inhibit fungal growth (11).

The amount of atmospheric moisture generated by the occupants of a household varies with the number of persons, their ages and lifestyles. Typical moisture emission rates for a four-person household range from 5

to 10 litres per 24 hours from breathing, cooking, personal and dish washing. As much again may be added by washing and drying clothes, and use of a paraffin or bottled gas heater for one evening will generate 1-2 litres of water (11). In addition to this internally generated moisture, the incoming air will bring with it a quantity of airborne moisture which depends upon the outdoor temperature and relative humidity.

The absolute quantity of moisture in the air is measured either as a concentration (g/kg dry air) or, more commonly, as vapour pressure (millibars). The temperature of the air determines the vapour pressure at which condensation will occur, and this saturation vapour pressure falls with decreasing temperature. The ratio of the actual vapour pressure (which is independent of temperature) to the saturation vapour pressure (which is not) is the relative humidity, usually expressed as a percentage (12).

The relative humidity of outdoor air is usually high, particularly in the winter months. Under normal circumstances, the air inside a dwelling is warmer than the air outside and incoming air, as it warms, is able to absorb moisture from the house fabric. The quantity of moisture which can be removed in this way depends partly on the rate of ventilation and partly on the

temperature difference between the indoor and outdoor air. Controlled intervention studies by the Building Research Establishment in poorly insulated damp flats in Stirling (Sanders C, personal communication) have established that if heating is inadequate, increased ventilation alone is unlikely to have a substantial impact on indoor relative humidity. Provision of free heating, with or without extractor fans, was sufficient to lower the internal relative humidity and remedy the problem.

In practice, however, the balance between heating, ventilation and moisture production provides only a partial explanation for the occurrence of damp patches on walls. Studies of dampness complaints in five local authorities in England and Wales (13) found that additional heating made little difference to the problem except in bathrooms. Two-thirds of the living rooms studied were damp, but all were heated. This discrepancy highlights the importance of cold patches on walls where, even in a heated room, inadequate insulation may cause a local drop in temperature below the "dew-point" for the indoor air. Whereas the ambient relative humidity in the rest of the room may be well below 70%, patches of condensation tend to occur at the base of poorly insulated walls or overlying "cold bridges" in the building structure (14). Although these

patches may appear similar to rising or penetrating dampness, surface condensation is free of salts and therefore provides ideal conditions for fungal growth (11)

Assessment by professional surveyors of 1000 Scottish private sector homes built between the wars suggested that about one-third of the dampness detected was related to rising or penetrating moisture, and about two-thirds was due to condensation (15). In local authority "system-built" housing dating from the 1950's and 1960's, condensation is more common and is related to poor insulation, high thermal mass (which responds slowly to heat input), inappropriate and expensive heating systems, cold bridging in pre-cast concrete construction and excessive moisture production due to the use of bottled gas or paraffin heating in the home (13,14).

2.2.2. Mould Growth

Moulds are spore-bearing saprophytic fungi which grow on dead organic material and foodstuffs. Although moulds themselves are often tolerant of dry conditions, germination of spores is usually limited by the humidity of their microenvironment. Thus, most species will not proliferate in atmospheric relative humidities below 70%, although some can grow slowly at relative

humidities down to 65% (16). Mould fungi have a very wide tolerance of temperatures, and suitable nutrients are ubiquitous, so that in houses the accumulation of moisture due to rising or penetrating dampness or condensation provides conditions suitable for mould growth.

Mould fungi are present at all times out of doors on dead and decaying organic matter and in the soil. There is a seasonal variation in outdoor airborne spore counts with levels of 50,000 per cubic metre being typical of a summer garden (17). Occupational exposures which are implicated in allergic alveolitis, for instance the handling of mouldy hay, are associated with airborne spore burdens of a different order of magnitude, reaching 1,600,000,000 per cubic metre (18).

There is scant information on the extent to which indoor mould growth affects the composition of the air spora in the United Kingdom. It is only in the past decade that it has been recognized that the simple and widely used techniques involving open culture plates were invalid. These "settle" plates are relatively insensitive indicators of the prevalence of small spores such as Penicillium and Aspergillus, whereas large spores and clumps of smaller material precipitate preferentially onto the plate. The alternative is to

use a volumetric (Anderson) sampler which draws air past a series of culture plates (19,20).

A recent survey which used this technique in 60 occupied council houses in London and three Scottish towns (21) found considerable differences in the total airborne spore burden, not only between homes, but also on repeated sampling within homes. Spore counts ranging from less than 50 to more than 2000 per cubic metre were not unusual in repeated measurements from the same room. This variation is probably related to domestic activity, since spores are found in large numbers in house dust (100,000 to 1 million per gram of dust (11)). Building and decorating work may also release large numbers of spores.

In homes with no visible mould, airborne spore counts were generally less than 200 per cubic metre. Where mould was present in another room in the house, most counts in non-mouldy rooms were in a similar range, but more high counts were observed. In rooms with visible mould, counts were generally in the range 1000-2000 per cubic metre, with further skewing of the distribution towards high values. Fungi belonging to 37 different genera were identified in the indoor air. Many were similar to those normally found out of doors (22). Penicillium, Cladosporium, Aspergillus and Sistotrema

species were found in more than half of the air samples, and all of these except Sistotrema were also isolated from wall surfaces. These results indicate that mould growth on walls does increase the indoor spore burden, although to a modest extent by comparison with outdoor concentrations.

Although it is valuable in comparing different homes, volumetric sampling may underestimate the true exposure of mobile human beings to mould spores. Spores may be released from house dust by movement in the room and enter convection currents around the warm body, which are estimated to contribute 10% of inspired air (22). Furthermore, the absolute spore count due to any one species, or to all species combined, may be of little clinical and epidemiological relevance, if spores from different species have different allergenic potential (23), or if hypersensitivity reactions can also be provoked by non-viable spores, which predominate, for example, in the air of some agricultural environments (24).

2.2.3. Damp, Mould and Respiratory Disease

Although dampness and mould growth have been suggested as causes of a wide range of disorders, including arthritis, anxiety states, gastrointestinal upset and skin rashes, most of the literature relates to possible

links with respiratory disease (5). The effect of the relative humidity of the air upon the incidence of respiratory disease has been considered, both in its own right, and as a determinant of levels of house dust mites or fungal moulds.

Green (25) reviewed eight studies in schools or workplaces where a comparison was made between the incidence of upper respiratory illnesses among the occupants of humidified and unhumidified buildings in the same city. The balance of the evidence was in favour of a lower incidence at relative humidity levels of 40% or more. Relative humidities in the unhumidified buildings were mostly in the range 20-30%, which is drier than in many centrally heated homes. As the subjects were in the buildings for only eight hours a day, the most likely mechanism for any effect of humidity was on the transmission of infection. Drying and cracking of the nasal mucosa may reduce host resistance at low relative humidities (25). On the other hand, studies of the viability of viruses in droplet spray at different relative humidities have suggested prolonged survival in more humid conditions (26,27). Animal experiments suggest that 50% relative humidity may be an optimum for limiting the infectivity of atomized influenza virus (28). Thus, both low and

high relative humidities may facilitate transmission of upper respiratory viral infections.

In contrast to these surveys in the workplace, studies of conditions in the home have consistently found a positive relationship between reported dampness or high relative humidity and reports of respiratory disease among the occupants. In studies of adult respondents, associations have been described between damp bedroom walls and wheeze (8) and between cold, damp homes and impaired ventilatory function (29). Confounding by smoking, occupation and social factors potentially complicates such studies, but after taking these factors into account, two Scandinavian studies report a significant relationship between cold, damp homes and respiratory symptoms (30) or lung function (29). No objective information about the home environment was obtained, so it is possible that the reporting of housing conditions was biased by awareness of symptoms. Furthermore, the Scandinavian studies were unusual, and possibly suspect, in that neither found an independent effect of smoking upon respiratory health.

A recent survey of 597 families with children in Glasgow, Edinburgh and London (31) found that adult respondents (mainly women) who reported their home to be damp or mouldy were more likely to report persistent

cough or wheeze, but these differences did not reach conventional levels of statistical significance and were not adjusted for age.

Studies of children are less prone to confounding in that the effects of active smoking (at least among primary school children) and occupational exposures can be excluded. Children are likely to have moved house less often than adults, and may be more susceptible to environmental challenges. A questionnaire survey of 5301 Swedish children aged 0-16 years (32) found an increased occurrence of persistent coughing, allergic rhinitis and allergic asthma (as reported by parents) among the children living in homes damaged by dampness. This was independent of residential area, type of dwelling and parental smoking. Questionnaire data were validated in a subsample of children by interview with a clinician and visits to the home by health inspectors, but no objective medical investigations were performed.

In the course of studies into the health consequences of nitrogen dioxide emissions from gas cookers, Melia et al. monitored ambient temperature and relative humidity for one week in the bedrooms of 156 primary school children in Cleveland, UK (33). In a subsequent interview with the parents, lower respiratory symptoms

were more commonly reported for the children from more humid bedrooms, but the effect of temperature independent of humidity was negligible. The response rate was only 44%, so it is possible that families who were aware of dampness in the home and who suspected a link with symptoms in their child might be overrepresented in the study. No objective medical data were obtained, so that the influence of reporting bias could not be assessed.

An alternative assessment of the home environment was used in a study of health and housing conditions in northwest Edinburgh (34). Information obtained at interview suggested that respiratory symptoms, particularly wheeze, were more common in children from homes reported to be damp, confirming my own study in the same area (1). No significant relationships were found for symptoms among adults. Independent assessments of dampness were made by environmental health officers (EHOs) who were blind to the questionnaire information. Using the criteria for dampness normally used to assess applications for rehousing, they found a high degree of concordance between EHO assessments and reports of dampness by the residents, and the association between dampness or mould growth and respiratory symptoms in children remained significant. However, with only 101 children

in the study, confounding effects could not be fully evaluated.

A larger study by the same team included 1169 children living in Edinburgh, Glasgow and London (31). Wheeze was more commonly reported for children in mouldy homes (prevalence 27%) than in non-mouldy damp homes (19%) and homes with no damp or mould (16%). Similar relationships were found for persistent cough. Both cough and wheeze showed a significant dose-response relationship with the severity of dampness, as assessed by environmental health officers, but their associations with total airborne mould spore counts (measured in three rooms on one occasion) were less strong. The results were adjusted for a range of confounding variables, but not for age. Biased reporting of child symptoms by parents remains a possible explanation, even of the relationships between symptoms and EHO assessments of dampness, because of the correlation between subjective and objective measures of dampness in the home. However, the absence of any association between adult symptoms and dampness in the same study argues against this.

In addition to this rather sparse epidemiological evidence concerning direct measurements of dampness or relative humidity, there is a substantial literature

supporting mechanisms whereby these conditions could affect respiratory health. In general, these observations are of value in establishing that a causal link might exist, but they are less useful for assessing the extent to which it actually applies in the community.

Studies of asthmatic patients have established by skin tests and nasal challenge that the majority exhibit immediate (Type 1) hypersensitivity to house dust (35). The faeces of house dust mites (Dermatophagoides pteronyssinus and Dermatophagoides farinae) are now recognized as the major source of allergenic material in house dust, which may contain up to 250,000 such pellets per gram of dust (36). The ecology of these species is well understood (37), and their proliferation is not limited by available foodstuffs, but by the temperature and relative humidity of their microenvironment. Mites can tolerate ranges of 17-32 deg C temperature and 55-80% relative humidity, and proliferate most rapidly at 25 deg C and 75-80% RH. In heated homes during the winter, the relative humidity falls below 45%, which effectively limits the degree of colonization by mites. (The figure of 45% is lower than the 55% mentioned above because the humidity in bedding is raised by the presence of a sleeping body.) Thus it is only the relatively humid homes which support large

concentrations of house dust mites (38), and it may be extremely difficult to eradicate mites from damp bedrooms, even in the context of a controlled trial (39).

While the concentrations of house dust mites and their faecal allergens are clearly determined by the temperature and relative humidity of the indoor environment, it is less well established whether such variation affects the prevalence or severity of asthma. In a case-control study of 25 newly diagnosed Danish asthmatics who were sensitive to house dust, Korsgaard found a higher mite count in the bedding of cases than that of 75 controls (40). A dose-response relationship was evident, and he estimated that about 60% of such cases were attributable to high levels of exposure. In contrast, a similar study in the south of England found no difference in the mite content of house dust from the homes of 176 asthmatics and 10 control homes (41). A prospective study of allergic symptoms among infants with a family history of atopy found no correlation between mite antigen concentration in house dust and wheezing in the first year of life (42). Removal of adult asthmatics to effectively mite-free environments in hospital has been demonstrated to relieve symptoms and reduce non-specific bronchial reactivity (43), but controlled trials of less drastic preventive measures

have been disappointing (35,39). Thus, although the aetiological importance of house dust mites in asthma is undisputed, it remains unclear how important are the variations in exposure normally encountered in the United Kingdom.

The possibility that airborne mould spores might have a causal role in asthma and hay fever was first proposed before the Second World War and became widely accepted in the 1950's (44). However, a review in 1981 pointed out that much of the evidence was anecdotal and the literature was inadequate and controversial (45). Type 1 cutaneous hypersensitivity reactions to mould extracts provided the best evidence of a causal link, but their interpretation was confused. False negative results might arise from the non-standardized methods of preparation, the restricted range of mould species tested, and the poor potency of many extracts. Spurious positive results might be due to cross-allergenicity, and even when skin tests were positive, nasal provocation tests were often negative (45).

The proportion of asthmatics with cutaneous hypersensitivity to extracts of mould fungi is lower than for house dust mite, but such reactions are not uncommon. Reported prevalence estimates vary from 3-4% in Sweden to 80% in the U.S.A. (45). Over 40% of

asthmatic patients in New Zealand were found to have strong skin test reactions to Alternaria, Cladosporium and Aspergillus species (46). Among 656 asthmatic patients attending an immunological out-patient clinic in London, 16% had positive skin tests to Aspergillus fumigatus, and 21% to other mould species (47). The species tested were Alternaria, Aspergillus terreus, Cladosporium, Merulius (dry rot), Sporobolomyces and Candida (yeasts). Overall, four out of five patients had multiple allergies, and almost all of those allergic to moulds were also allergic to house dust mites, so the independent contribution of mould allergy to their symptoms was difficult to determine.

In a detailed longitudinal study of eight Dutch asthmatics known to be allergic to moulds, pulmonary complaints were more common when outdoor mould spore concentrations were high, but no association was found with indoor concentrations (48). Positive evidence of mould allergy and symptoms attributable to domestic mould spores comes from a case-control study of 72 adult asthmatics and 72 controls matched for age and sex (49). Nineteen cases and nine controls reported visible mould on the walls of their homes, and there was a significantly higher prevalence of positive RAST to Penicillium among the cases reporting mould in their home. These results tentatively suggest that domestic

mould spores may be capable of invoking species-specific Type 1 hypersensitivity in a minority of asthmatic patients. The relationship of mould growth to symptoms remains uncertain, because of potential confounding by other aspects of the housing environment (in particular, humidity and its effect upon house dust mite populations), and because the reporting of visible mould in the home may differ according to disease status, due to a tendency for asthmatics to seek an identifiable cause for their complaint in their home environment.

2.2.4. Prevalence of Dampness

Although no rigorous definition of dampness has been applied in a representative sample of homes, estimates of the prevalence of dampness and related problems are available from several large-scale surveys in Great Britain. The 1981 English House Condition Survey (50) covered a sample of 4553 houses drawn from the stock of 16.8 million houses built before 1976. Dampness resulting in mould growth, or damage to decorations, floors, carpets or furniture affected 18% of owner-occupied homes, 33% of privately rented homes and 26% of local authority accommodation. Throughout the country, an estimated 2.5 million households were thus

affected by dampness, and a further 6 million were troubled by condensation on window panes.

A report by the Scottish Office in 1984 (15) compiled information from local authorities and field surveys and concluded that condensation affected between one-quarter and one-third of the Scottish public sector housing stock and approaching one-fifth of private sector housing. Overall, 15-20% of Scottish homes were affected by mould growth. Comparable figures were obtained in a more recent survey of the condition of the Glasgow housing stock (14).

2.2.5. Dampness as a Local Political Issue

Figures from national surveys indicate the scale of the problem, but do not adequately describe the variation in prevalence of dampness and mould growth, particularly in the local authority housing stock. Large "system-built" estates dating from the 1950's and 1960's are a feature of most of Britain's cities. Similarities in construction can lead to common problems of structural disrepair or poor insulation which result in a geographical clustering of dampness complaints and the emergence of dampness as a local political issue, which often acts as a focus for more general discontent about housing conditions. Over the past decade, many residents' and tenants' groups

throughout the country have campaigned for improvements, and several have conducted surveys to highlight the prevalence of dampness or the related problems of poor insulation and inefficient or expensive heating systems (51-55).

Residents in these areas often perceive housing as a major determinant of their health. In the Spitalfields area of London's East End, poor and overcrowded housing was considered by the tenants to be the most important health problem in the ward (56). Particular emphasis was placed upon uncleared rubbish, structural and sanitary disrepair, lack of amenities and dampness. A similar survey in the Pilton area of northwest Edinburgh found that damp housing was the leading health-related problem in the eyes of the community (57). The identification of housing as a health hazard appears to be strongly related to the popularity of the local housing estate. Among local authority tenants in Tyneside, 43% of the residents in estates that were difficult to let attributed at least one respiratory symptom to their housing, whereas on more desirable estates only 10% did so (58).

Recognition of these perceived health problems has led some community action groups, either alone or with advice from local academics, to investigate the

association between dampness or mould growth and symptoms, particularly of respiratory disease. Some have simply sought to document the high prevalence of both dampness and respiratory symptoms (59). Others have pursued an epidemiological approach and demonstrated a higher prevalence of symptoms among the occupants of damp homes than among tenants unaffected by dampness (54,55,57,60,61).

These surveys are generally limited by the small numbers of households studied. Few take due account of possible selection effects in the allocation of housing within the rented sector (58), and rigorous control of confounding by age and smoking receive less attention than would be required in a formal epidemiological enquiry. With two exceptions (57,61), no objective data were collected. Nevertheless, the fact that these studies were conducted at all serves as a reminder of the importance attached to damp housing by those affected. Furthermore, the consistent finding that respiratory symptoms are more common in damp housing, particularly among children, suggests that there is a need for more rigorous evaluation of the effects of dampness on health.

2.2.6. Dampness and Public Health Legislation

The principle of controlling health hazards by legislative action in the housing sector dates back to the 1855 Nuisance Removal and Diseases Prevention Act, which permitted local authorities to close a house which was judged "unfit for human habitation". In pioneering such legislation, the Victorians accepted the prevailing "miasmatic" theory that noxious vapours were the cause of transmissible diseases, a concept which may not be entirely irrelevant to public perceptions of the link between dampness and ill-health in the latter half of the twentieth century.

The loosely defined concept of "fitness" remained a keystone of sanitary policy, but it was not until 1919 that a systematic definition of a fitness standard was attempted in the Manual on Unfit Houses and Unhealthy Areas (62). The 1919 standard remains the basis of the present fitness standard in England and Wales (63) and the present tolerable standard in Scotland (64). These both refer specifically to freedom from damp, and the Dennington Committee which developed the English standard added the explanatory note "dampness not so pervasive as to be a threat to health" (65). This link to health is maintained in the 1987 Consultation Paper (66) which suggests that fitness for human habitation

should imply freedom from "dampness prejudicial to the health of the occupants". The same consultation paper suggested a more stringent "target standard" which includes adequate heating and thermal insulation.

Professional responses to local anti-dampness campaigns have come not only from interested academics, but also from local law centres. Lawyers have assumed the link between dampness and ill-health to be self-evident, and have attempted to help both individual tenants and groups of tenants sharing a single block of flats. The effectiveness of collective legal action was highlighted in July 1986 when three tenants brought an action against Birmingham City Council (the largest landlord in England). Birmingham Magistrates Court ruled that Beale House, a "system-built" nine-storey block in Ladywood, Birmingham, was a Statutory Nuisance because it was "prejudicial to health" under Section 92(1)a of the 1936 Public Health Act (67). The main problem in this and two adjacent blocks was condensation and mould growth related principally to poor insulation. Remedial works to the three buildings totalled over £1 million, but the High Court judge, upholding the magistrates decision, commented that "this case should not be regarded as a precedent for a schedule of works of the nature I have indicated". Birmingham City Council later reported that up to

40,000 of its tenants were potentially affected by such a precedent (68).

This success in the courts was achieved on the basis of expert evidence that damp, mouldy conditions can cause or exacerbate health problems, without any rigorous evaluation of the extent to which they actually do so in the community. With the large sums of money involved in refurbishment, it is clear that any remedy for dampness in the local authority stock as a whole must be based on a planned use of scarce public funds. This requires an assessment, not only of the costs and benefits of correcting dampness, but of alternative uses for the same resources, including the provision of more (rather than better) housing. For instance, at the time of the above judgment, there were 11,000 pre-war houses in Birmingham without inside lavatories, over 8% of the total housing stock (68).

2.2.7. Synopsis

Dampness, loosely defined, affects an estimated 20-25% of homes in Britain. Rising and penetrating moisture are less commonly the cause than surface condensation, which provides ideal conditions for mould growth. Indoor air usually contains fewer fungal spores than are found out of doors, but there is some evidence that

mould growth in the home affects the quality and quantity of the airborne mycological flora.

Both low and high ambient humidity have been associated with respiratory disease in epidemiological studies. The proliferation of house dust mites and fungal moulds in conditions of high humidity supports a link between damp housing conditions and childhood asthma, but such a relationship has not been rigorously investigated in epidemiological studies. The problem of reporting bias is of particular concern in view of the widespread identification of dampness as a hazard to health by the tenants of affected council estates.

Current and proposed standards of "fitness for human habitation" stipulate freedom from dampness that is prejuducial to health. As dampness appears to be so prevalent in the British housing stock, firm evidence that it is a health hazard would have major implications for the proportion of homes deemed "unfit" and, thereby, eligible for closure. Although a causal link between dampness and ill-health has been successfully claimed in legal proceedings, the development of a rational policy for improvement of the nation's housing stock requires a quantitative estimate, not only of the health effects of dampness,

but also of hazards related to other remediable housing conditions.

2.3. Environmental Tobacco Smoke Exposure

2.3.1. Measurement

Tobacco smoking in indoor environments increases the concentration of suspended particulate matter of respirable size in indoor air, and the level of many constituent chemicals, including nicotine, carbon monoxide and nitrogen dioxide. Suspended particulates have been most widely used for environmental monitoring, and such studies have demonstrated that in homes with two or more heavy smokers, mean levels of total suspended particulates may exceed the United States Air Quality Standard (260 micrograms per cubic metre) designed for control of outdoor air pollution (69). Presumably, peak concentrations are considerably higher.

Personal exposure to tobacco smoke can be assessed by portable monitoring equipment or by the use of biological markers. The former has the advantage of measuring exposure directly, independent of metabolic differences between individuals, but is expensive, time-consuming and inconvenient for the subject. Using

personal monitors, Spengler et al. have confirmed that non-smoking adults exposed to tobacco smoke in the home have substantially increased mean daily exposure to respirable particulates (70). These findings are consistent with comparisons between smoking and non-smoking areas in offices, public places and transport vehicles (4).

A number of biochemical markers have been used to estimate passive smoke exposure. Thiocyanate in body fluids, carboxyhaemoglobin in blood and carbon monoxide in expired air are influenced by other factors and do not adequately distinguish between those exposed and unexposed to environmental tobacco smoke (71). Neither nicotine nor its metabolite cotinine are present in body fluids in the absence of tobacco smoke. Nicotine is rapidly metabolized to cotinine, which is the marker of choice for quantifying long-term exposure. Its biological half-life is approximately 20 hours, and it can be assayed in concentrations as low as 0.1 ng/ml by gas-liquid chromatography (72). Typical levels in actively smoking adults are 300 ng/ml, whereas concentrations up to 15 ng/ml can reasonably be attributed to passive exposure. Concentrations in saliva are in approximate equilibrium with those in blood (73) and have been used to measure the degree of passive smoking among children, adolescents and non-

smoking adults (73-77). Other studies have estimated cotinine concentrations in serum (78) or urine (79-82).

The marked differences between cotinine levels in non-smokers and smokers have been used to validate self-reported smoking behaviour (74,76). Most studies of non-smokers have reported a dose-response relationship between cotinine level and the number of smokers in the household. The within-subject variability of cotinine in saliva was assessed by Jarvis et al. in non-smoking adolescent girls (83). Levels showed a fairly high degree of consistency, with a correlation coefficient of 0.75 between measurements taken one year apart. These observations confirm that the concentration of cotinine in biological fluids is a repeatable and valid measure of tobacco smoke exposure.

2.3.2. Effects upon Respiratory Disease in Children

The role of passive smoking as a determinant of respiratory disease in children has been extensively investigated using questionnaire information to estimate exposure. These studies have been the subject of several comprehensive reviews (4,6,84-86) and will not be discussed in detail here. No studies have been published in which an objective measurement of passive smoke exposure was related to disease outcomes.

Prospective studies have shown that the effect of parental smoking upon respiratory infection in infancy is strong and consistent. It appears to be related to environmental exposure, rather than intrauterine influences from maternal smoking, because in China, where smoking among women is rare, paternal smoking is associated with an increased rate of hospitalization for respiratory disease in infancy (87). The effect of maternal smoking upon respiratory illnesses declines with the age of the child up to the age of three years (88).

The evidence for an association between respiratory symptoms and environmental smoke exposure in children of school age is less clear. Most epidemiological studies have been cross-sectional in design and the investigation of passive smoking effects has been opportunistic. The information about parental smoking in many studies is therefore rather crude. Although most find some association between respiratory symptoms and parental smoking, evidence of a dose-response relationship is inconsistent, particularly in the smaller studies (89,90). Few studies have been able to take into account the wide range of potential confounding effects (91). In older primary school children, active smoking, even on an experimental basis, may have substantial effects upon the prevalence

of respiratory symptoms (92,93) and potentially confounds the investigation of passive smoking.

Relatively few studies relate measurements of pulmonary function to passive smoking by children. Although most demonstrate an adverse effect of environmental smoke exposure, this is not always statistically significant. Many of the earlier studies were of a cross-sectional design, but more recently there have been several longitudinal investigations demonstrating a reduction in the growth of lung function among children exposed to tobacco smoke (94-96). Cumulative lifetime passive smoke exposure, determined retrospectively by questionnaire, has recently been found to relate to decreased ventilatory function in nonsmoking young adults (97). These findings imply that cross-sectional studies in young children may not be the most sensitive method of detecting long-term pulmonary consequences of passive smoking. On the other hand, ventilatory function in adolescents and young adults may be influenced by many additional factors, such as occupation and previous active smoking (98), which can be effectively excluded in younger age-groups.

Evidence of the effect of passive smoke exposure on the occurrence of middle ear effusion has emerged from three recent case-control studies of children admitted

for grommet insertion (99-101). In one, the relative risk was significantly raised only at high levels of parental smoking (99). Referral and admission criteria for middle ear effusion appear to be determined to a substantial extent by the health culture of the family (102), so the interpretation of studies based on hospitalized patients is potentially complicated by selection bias, which might result in either a spurious relationship with parental smoking, or an underestimate of a true effect.

Five cross-sectional surveys of general population samples have reported upon the association between middle ear effusion and passive smoke exposure (103-107). Only one (103) found a significant association and suggested that the risk increased with age. If this is so, it might explain the negative results of the other two studies which were based on pre-school children.

2.4. Childhood Asthma

2.4.1. The Nature of the Disease

Cross-sectional studies of primary school children have demonstrated that a tendency to wheeze is one of the commonest chronic conditions of childhood. Prevalence

figures at various ages obtained from British studies have been reviewed in two recent papers (108,109). Estimates of the annual period prevalence of asthma or wheezy bronchitis at seven years of age range from 8% in a British national cohort (110) to 11% in Melbourne, Australia (111) and Tyneside, U.K. (112), and 12% in Southampton, U.K. (113). Rigorous comparisons cannot be made due to variations in the case definition and methods of ascertainment used in each survey.

There has been considerable controversy in the past as to whether all wheezing in childhood is part of a single disease spectrum, or whether asthma and other forms of wheezing illness should be regarded as separate diseases with different epidemiological and clinical characteristics. Early studies of the epidemiology of childhood asthma (114-116) found that this diagnosis was more common among children from upper class families. The opposing social class trends for asthma and for wheezy bronchitis were considered to indicate different diseases (114). However, among British children born in 1958 and 1970, there was little variation across social groups when all wheezing illnesses were combined (110,117), and reports of wheeze in a recent symptom questionnaire did not vary with parental social class (113). Social and family factors have been shown to be determinants of the

treatment received by wheezy children (113), and it has been suggested that, in the past, social class differentials in disease labelling could account for apparent differences in the epidemiological characteristics of asthma and wheezy bronchitis (119).

More recently, there has been a growing consensus that all forms of wheezing should be regarded as part of a single spectrum of disease, embracing both asthma and wheezy bronchitis (119). This is based on observations that, regardless of diagnostic label, almost all wheezy children eventually develop some manifestation of an atopic disposition (120), and that the response of wheeze to bronchodilator therapy is similar in cases labelled asthma and those formerly diagnosed as wheezy bronchitis (121). These considerations are of clinical significance because there is continuing concern that reluctance to diagnose wheeze as asthma results in widespread undertreatment and unnecessary morbidity (109,121).

2.4.2. Public Health Significance

Much of the attention focused upon asthma in the general medical press has highlighted the problem of potentially avoidable asthma deaths, and the recent trends of increasing mortality in some countries, including England and Wales (122,123). While this is

undoubtedly an important issue, the number of asthma deaths is extremely small, particularly in childhood. The main impact of asthma on the public health is in terms of the recurrent morbidity experienced by patients and the burden that it imposes on health services.

Childhood asthma is a major cause of recurrent school absence (109), which can be reduced by adequate treatment (121). Exercise-induced attacks are experience by over three-quarters of asthmatic children, and many of these may have resulting disruption of their sports activity (124). Despite the fact that asthma is underdiagnosed and undertreated, inhaled bronchodilators are currently the drug preparations most commonly used by children, accounting for almost 10% of all days of drug use, with a peak at 5-7 years of age (125).

As expected, the use of medical services by asthmatic children increases with the severity of their complaint (118). Overall, at 8-9 years of age, about half visit their general practitioner for wheezing illness in the course of a year. An increased rate of general practice consultations for respiratory complaints appears to precede the date of diagnosis, suggesting that frequent attendance with respiratory symptoms should be

considered an early indicator of asthma (126). It has been suggested that chronic nocturnal cough may be a manifestation of hyperreactive airways, even in the absence of wheeze (127), and that this symptom may respond to bronchodilator therapy (128).

Although many asthmatic children do not come into contact with hospital, those that do impose a significant burden on both outpatient and inpatient services (118). Admissions for asthma accounted for one in twenty of all hospital admissions of children aged 5-9 in England during 1985 (129). As with mortality, there is concern that the rate of admission is rising (123,130). This trend does not appear to be due to a change in diagnostic labelling, but a more liberal admissions policy may have been a contributory factor during the seventies (131). More recently, the acceleration in admission rates has not been associated with any change in the severity of hospitalized attacks, nor the proportion of readmissions (132). As the prevalence of childhood asthma does not appear to be increasing (108), this implies that an increasing proportion of wheezy children may be experiencing severe attacks.

Recently there has been renewed interest in the possibility that chest illness in childhood may have

long-term consequences for respiratory health, and may be a cofactor in the development of fatal and disabling chronic respiratory disease in middle age (133-137). Although many wheezy children appear to "grow out of" their asthma (110,138), those that do not are at risk of cough and phlegm in early adulthood (137,138), and it has been suggested that airways hyperreactivity in early adulthood may predispose to more rapid development of irreversible airways obstruction (139). These observations suggest that the significance of childhood asthma to the patient and the community may need to be assessed from a much broader perspective than has hitherto been the case.

2.4.3. Aetiology

If asthma is on the increase, then the factors which might determine changes in incidence or prevalence are poorly understood (123). Apart from the well recognized association with a personal and family history of atopic disease, few factors have been found to be associated with wheeze in childhood (110,117). A consistent association with bronchitis and pneumonia may reflect the greater susceptibility of asthmatic children to all forms of chest illness (110). The relationship with parental smoking has been discussed in the abovementioned reviews of passive smoke exposure

(4,6,84-86) and the findings are inconsistent. The failure to find powerful determinants at the level of the individual or family group has led to a suggestion that the important determinants of asthma may lie at a different level, among environmental factors affecting whole communities (119).

Support for the importance of environmental determinants comes from studies of unaccultured populations who become exposed to "Western civilization". The prevalence of asthma (11%) and atopic disease (0.1%) among native Tokelauan children are low by comparison with Tokelauans living in New Zealand (25% and 8.5%, respectively) (140). Exercise-induced bronchospasm was found in 0.1% of rural Xhosa children in South Africa, but was present in 3% of urban Xhosa children of the same genetic stock (141). Dietary sodium is one feature of the accultured environment for which there is evidence of a link to asthma, at least in adults (142).

Whereas the determinants of the asthmatic trait are poorly understood, potential triggers for attacks of wheeze are well documented. Cold air, certain air pollutants, exercise, emotion, allergen exposure and respiratory infection may all provoke episodes of bronchospasm in susceptible individuals. In children,

most attacks of wheezing appear to be precipitated by viral respiratory infection rather than airborne allergens, even among atopic subjects (143,144). Temporal variations in hospital admissions for asthma in children correlate closely with the timing of school holidays and half-term breaks, suggesting that the incidence of attacks is dependent upon circulation of respiratory viruses among children at school (145). Local epidemics of asthma admissions have been attributed to changes in the weather (146) and the consequent increase in outdoor concentrations of airborne fungal spores (147), but these circumstances appear to be exceptional and probably do not explain more than a small fraction of all asthma attacks.

Although only a minority of wheezy children exhibit immediate (Type 1) cutaneous hypersensitivity to common environmental allergens at the age of seven, the majority do so at some time during childhood or adolescence (120). House dust mite allergy is the most prevalent atopic disposition, and chronic exposure to house dust mite faeces has been proposed as a determinant of chronic airways hyperreactivity (35). However, trials of mite eradication in childhood asthma have been disappointing, perhaps because the measures which are acceptable to parents and their offspring are inadequate to eliminate exposure (35,39). More

promising results have been reported from a small group of severely asthmatic children with house dust mite allergy who stayed in an effectively mite-free environment at high altitude in the Italian Alps for eight months (148).

2.4.4. Bronchial Challenge Tests

The concept of asthma as a chronic underlying susceptibility to wheeze in response to a variety of stimuli has led to investigation of techniques for the detection of "non-specific bronchial hyperreactivity" (149). A variety of physiological stimuli have been used, including challenges with cold dry air, aqueous aerosols, or exercise, but most published work relates to the use of graded doses of a pharmacological challenge, such as aerosols of histamine or methacholine. A number of indices of ventilatory function may be used to assess the consequent change in airways calibre, though forced expiratory volume in one second is most widely used (149).

One essential limitation of all such techniques has been highlighted by Scadding (150). Although individual responses to different challenges tend to be correlated (151), failure to respond to any one stimulus does not preclude a capability to respond to another. Thus, all tests have limited sensitivity to the full spectrum of

asthma. An exclusive definition of the disease on the basis of bronchial reactivity tests would have to assess each individual's response to all known precipitants of asthma (150).

A second limitation is the absence of any "gold standard" against which positive results can be validated. Thus, with pharmacological challenges, the response of normal airways to high doses of the agent cannot be adequately defined. One way around this problem has been to treat the threshold concentration which causes bronchospasm as a continuous variable and study it as a pathophysiological outcome in its own right, without attempting to define a cut-off point for asthma (151). Validity is less of a problem with physiological challenges such as exercise, where the range of intensity can be related to everyday activity and a positive response may be considered of direct relevance to the patient.

Recent studies have demonstrated the feasibility of histamine challenge in 7-year-old children in Tyneside, U.K. (112), methacholine challenge in 7-year-olds in Southampton, U.K. (152,153) and 9-year-olds in Dunedin, New Zealand (154), and hyperventilation with cold dry air in schoolchildren in the U.S.A. (155). Exercise testing has a longer history in paediatric outpatient

practice and therapeutic research. A review in 1975 (156) suggested that a reduction in peak expiratory flow rate (PEFR) or forced expiratory volume in one second (FEV1) of 15% or more occurred in about 70% of asthmatic children within ten minutes of exercise. The optimal exercise challenge was 6-8 minutes free running, and the most sensitive indicators of changes in airflow were mid-expiratory flow rates, followed by FEV1 and PEFR.

In children, random errors in the measurement of ventilatory function are a potential source of false positive and false negative errors, but their consequences in the context of challenge testing have not been thoroughly assessed. The evidence suggests that the repeatability of changes in PEFR after exercise is rather poor; in one study of treadmill running, the coefficient of variation for duplicate measurements taken one week apart was 21% and for measurements separated by one month was 53% (157). Over a longer period of time, however, the degree of reactivity appears to follow the remitting and relapsing course of symptomatic asthma (158). Thus, it has been suggested that the exercise-induced change in PEFR might be of diagnostic value in general practice, particularly among children with recurrent respiratory symptoms which might be attributable to asthma (159).

Two epidemiological studies have investigated exercise-induced bronchial lability in a population sample in Britain. A recent survey of 503 primary school children aged 6-12 years in Sheffield (160) evaluated free running as a screening test for asthma. In a subsample of 229 children, the efficiency of the challenge was assessed by telemetric monitoring of heart rate during exercise (161). In all these children, the heart rate rose above 170 beats per minute during the six-minute exercise period. In the main study, a satisfactory test was completed by 434 children, of whom 22 had a history of wheeze in the past year, as reported by parents in a postal questionnaire. Eleven (50%) of the wheezy children and 14 (3.4%) of the remainder experienced a reduction of 15% in PEFR at both 5 and 10 minutes after exercise. After more detailed interview and examination, ten of the 14 "normal" children with exercise-induced bronchospasm were diagnosed as asthmatics (160).

Exercise-induced reduction in PEFR was also measured in a survey of 812 twelve-year-old children in South Wales (162). A reduction of 15% or more five minutes after exercise was found in 7% of the sample. This "reactive" group included 18 of 33 diagnosed asthmatics, 9/49 children with other forms of wheeze, 4/56 children with a history of wheeze in the past, 7/67 children with

other atopic disease, 5/59 children with a family history of wheeze and 12/548 other children (assumed to have no atopic disease or disposition). These results suggested a spectrum of abnormal airway responses to exercise, loosely related to asthma and other atopic disorders.

Another study of 75 siblings of asthmatic patients suggested that the correlation of exercise-induced bronchospasm and cutaneous hypersensitivity was poor; in less than half of the subjects with positive skin tests did PEFR fall by more than 10% after exercise, and only half of those with exercise-induced bronchospasm had positive skin tests (163). In common with the Welsh study, only half of the reactive children had received a diagnosis of asthma, despite the fact that their sibling had been so diagnosed. This raises doubts about the clinical significance of some of the positive results.

In summary, bronchial reactivity tests presuppose that the chronic susceptibility to wheeze in response to environmental and endogenous triggers can be assessed by challenging the airways with one specific stimulus. Physiological challenges may be limited by poor sensitivity, pharmacological challenges by uncertainty about their specificity. Few epidemiological studies

have utilized any form of challenge testing in primary school children, but treadmill exercise has achieved more widespread acceptance in hospital practice. In terms of achieved pulse rate, free running appears to be an adequate exercise challenge when applied to children in the community, and, because such activity is physiological, abnormal bronchoconstrictor responses may be considered to have intrinsic validity. However, false positive errors may arise from the limited precision of any measurement of ventilatory function, particularly among young children.

2.5. Middle Ear Effusion

2.5.1. Nature and Public Health Significance

Middle ear effusion, otherwise known as serous otitis media, secretory otitis media, otitis media with effusion, or "glue ear", is characterized by Eustachian tube blockage, negative middle ear pressure and the accumulation of a serous transudate in the middle ear cavity (164). It is a disease of the first decade of life which is often asymptomatic, but which may result in conductive deafness. There is concern that the resulting hearing disorder may impair language development and educational progress (165). Treatment

by myringotomy, adenoidectomy or tonsillectomy has increased substantially over the past two decades (166), and it has been suggested that this may reflect the acceptability of glue ear as a diagnostic label for children of middle-class parents whose educational performance is disappointing (167). Operation rates for glue ear increased by 74% in Oxford Regional Health Authority from 1975 to 1981, and this "surgical epidemic" continues (166).

Surgery for glue ear is most frequently performed between 5 and 7 years of age and is now the commonest reason for young children to be admitted to surgical wards (166). Rates of surgery vary widely between regions (168), and in some areas of England and Wales, glue ear is the commonest reason for hospital admission of any kind among children of this age (166). Presentation and referral for surgical treatment appear to be determined to a large extent by the "health culture" of the family (102) and by local clinical practice (168), so the relationship of operation rates to disease prevalence, over time and between regions, remains obscure. However, secretory otitis media was recognized in the mid-nineteenth century and frequently described as "common", so the rise in surgical activity is likely to be primarily a medical care phenomenon (166).

2.5.2. Aetiology

Despite its long history, there is little agreement about the aetiology of glue ear. Black (169) reviewed aetiological theories proposed over the past century, including climate, nutrition, heredity, lifestyle, social conditions, acute or chronic illnesses, allergy and iatrogenesis. He concluded that prevailing beliefs about the aetiology of glue ear reflected the current views about aetiology of disease in general, and that few of the proposed causes commanded any scientific support.

Recent studies have consistently implicated upper respiratory infection as a risk factor for middle ear effusion (164,170,171), and this may account for the seasonal variation in prevalence and the association with day care outside the home (171,172). However, as upper respiratory infections are ubiquitous among young children, other factors must be operating to determine individual susceptibility. The major underlying mechanism in the pathogenesis of glue ear is thought to be Eustachian tube blockage, which may in turn be influenced by anatomical factors (such as cleft palate, craniofacial abnormalities and adenoid hyperplasia), infection, allergy and mucociliary function (164).

One case-control study which investigated a wide range of factors concluded that the most striking finding was the similarity of cases (attending for grommet insertion) and controls (100). However, cases were more heavily exposed to cigarette smoking in the home. Another case-control study suggested that catarrh, atopy and passive smoking might have joint effects upon the prevalence of middle ear effusion, and that the risk associated with passive smoking was particularly marked at high levels of exposure (99). A third case-control study supported a link with parental smoking (101). However, the association with passive smoke exposure has been confirmed in only one (103) of five population based studies (103-107).

2.5.3. Measurement

Clinical examination by pneumatic otoscopy, audiometric tests of hearing acuity, impedance tympanometry and acoustic reflex testing have been used for clinical diagnosis of middle ear effusion and for screening purposes. The considerable variation in appearance of the tympanic membrane in ears with effusion, and the intra- and inter-observer variability in otoscopic assessment limit the value of pneumatic otoscopy for epidemiological research. Pure-tone audiometry is of limited diagnostic value in middle ear effusion, since

other causes of hearing loss may be present, but it does provide an indication of the severity of the condition and its likely consequences (164).

Since its introduction into Scandinavia (173) and later into the U.K. (174), impedance tympanometry has become widely used as a diagnostic and screening tool in young children, and automated equipment is now available to permit fully objective measurement. (A description of the method and definition of terms appears as Appendix C). The early classification of tympanograms by Jerger (175) into Type A (peak at normal middle ear pressure), Type B (no peak) and Type C (peak at reduced middle ear pressure) has been widely accepted. Fiellau-Nikolajsen has refined and quantified these distinctions in terms of the middle ear pressure and relative gradient of the tympanometric curve (176).

The distinction between tympanograms with and without a definable peak has been validated as an indicator of fluid in the middle ear cavity by aspirating both ears of patients under anaesthesia for myringotomy (176-178). These are highly selected patients with persistent abnormalities, and the use of tympanometric findings from the "normal" ears of the same children is of questionable validity. Furthermore, there is concern that spurious false negative results may arise as the

Eustachian tube relaxes under anaesthesia, resulting in drainage of fluid into the pharynx (179). Subject to these reservations, the sensitivity of a Type B tympanogram varies between 69% and 87%, the specificity between 81% and 98% (176-178). Although this implies a predictive value of about 85% among hospitalized children (178), the predictive value in the general population is almost certainly much lower.

Ethical considerations obviously limit the scope for similar validation in the community setting, but studies have investigated the repeatability of tympanometric findings in children of primary school age. In a screening program in south London, 41% of children aged 5-6 years had abnormal tympanograms at the first test, but half had recovered spontaneously by the second test (180). In a series of monthly tympanograms among unselected 7-year-old children in Denmark, only 31% had normal Type A tympanograms on each of ten tests, 43% developed reduced middle ear pressure (Type C) but never developed an effusion (Type B). One quarter of the children had a Type B tympanogram at one or more tests, but in only 5% did this persist for more than five months (181). The point prevalence of Type B tympanograms varied from 3% to 9%, being highest in the winter and spring. In the same study, the sensitivity and specificity of a Type B

tympanogram at the first test were evaluated using as a reference standard the 5% of children with Type B tympanograms persisting for five or more months. This indirect validation gave sensitivity 65%, specificity 96% and predictive value 50% (182). No improvement in test performance was noted by including abnormalities of the acoustic (stapedius) reflex. This is probably as close as is feasible to a formal validation of impedance tympanometry in the community.

In summary, impedance tympanometry offers an automated and fully objective method of detecting middle ear effusion. Although seasonal variations in the prevalence of glue ear limit the repeatability of any one test result, the method is well suited to large epidemiological surveys. It thereby permits a study of the aetiology of this important condition, free from the selection effects which may complicate case-control studies based on children admitted for surgical treatment.

3. METHODS

3.1. Sample Selection

Ethical approval was obtained from the Paediatric/Reproductive Medicine Ethics of Medical Research Sub-Committee of the Lothian Health Board and from the Research Committee of the Department of Education, Lothian Regional Council.

A cluster sample of primary school children in their third (P3) year was chosen as follows. A random sample of one in three state primary schools within the Edinburgh city boundary was chosen from an alphabetical list provided by Lothian Regional Council. Catholic schools were included in the sampling frame. The headteachers of thirty-two schools were contacted and all but two agreed that their school could participate in the study. These two schools were not replaced. Headteachers of the thirty cooperating schools provided a list of the names and addresses of all children in the P3 year, which formed the target sample for the study. These children were aged $6\frac{1}{2}$ to $7\frac{1}{2}$ years in September 1986.

3.2. Questionnaire Survey

In the last week of November 1986, the children in each P3 class were given an envelope to take home to their parents. This contained an explanatory cover letter, a two-page questionnaire for completion by the parents, and a form of consent to the inclusion of their child in the remainder of the study (Appendix A). Completed questionnaires were returned in a sealed envelope to a collecting box in the classroom. The cooperation of the class teachers ensured prompt return of questionnaires and a high initial response rate. Children absent at the time of the launch were given a questionnaire on their return, and parents who had not responded after ten days were contacted by letter or telephone to maximize the number of replies.

The parents of 1095 children received a questionnaire and usable replies were obtained from 1012 (92%). Parental social class was determined from the current or last occupation of the head of the household, coded according to the 1980 Registrar General's classification (183).

Written consent to further tests was obtained for 941 children (86% of the target sample). Twenty of these children left school before the respiratory examination survey, and two of the smallest schools (accounting for

a further 20 children) were used for pilot studies of the respiratory examination protocol. The number of children eligible for inclusion in the clinical survey was therefore 901 (82% of the target sample), 892 (99%) of whom were eventually examined.

3.3. Respiratory Examination Survey

Each participating school was visited over the period January to June 1987 to perform clinical tests on the children from whose parents consent had been obtained. Where necessary, one repeat visit was made to test children absent due to illness on the first occasion. It was not possible to test four children due to repeated sickness absence, and five others were on holiday at the time of the examination.

Children were tested in pairs by the author, assisted by a research nurse. Each child was asked whether they had used an inhaler in the past 24 hours, and, if so, which type and at what time. Where possible, the child's test was rescheduled to ensure that at least six hours had elapsed since their last dose of inhaler. This was achieved for all children who were treated only with inhaled beta-2 agonists or sodium cromoglycate. Eleven children were considered to be

taking treatment for asthma which might have influenced the result of their spirometry. Five of these were long-term users of oral theophyllines or oral steroids, and the other six inhaled steroid preparations twice daily.

The test protocol consisted of the following:

3.3.1. Height

Standing height was measured with shoes removed, to the nearest centimetre below, using a standard measuring scale mounted on a board and placed vertically against a wall. To ensure standardization of measurements, the school's own scale was not used.

3.3.2. Baseline Spirometry

After a period of instruction and two practice attempts, each child performed three forced expiratory manoeuvres, according to the methods recommended by the American Thoracic Society (184). Tests were performed in the standing position and nose clips were not used. Two further expirations were performed if the two "best tests" of the first set of three were not within 5% of each other according to the best test criteria of the American Thoracic Society (i.e. the spirogram with the greatest sum of FEV1 and FVC) (184).

A "Compact" pneumotachograph (Vitalograph Ltd, Buckingham, U.K.) with a paediatric mouthpiece adapter was used to record each spirogram. This measures air flow through a resistive mesh, on the Fleisch principle, and determines volumes by flow integration. The following spirometric indices were calculated from each expiration: FVC, FEV1, FEV0.5, PEFR, FEF25-75%, FEF75-85%, FEF25%, FEF50% and FEF75% (A glossary of these abbreviations appears in Appendix B). Back-extrapolation was employed automatically in the calculation of zero time for forced expiratory volumes. The maximum value of FVC, FEV1 and FEV0.5 from the two best spirograms was recorded, but all flow rates were recorded from the best spirogram, according to the recommendations of the American Thoracic Society (184). In addition, for greater comparability with surveys which have recorded only peak expiratory flow rate, the maximum achieved PEFR was recorded (this was not always from the best spirogram).

The same instrument was used throughout the survey, and all expiratory manoeuvres were supervised by the author. At the start of each 2-hour session, the pneumotachograph was calibrated volumetrically using a 1-litre precision syringe. Three litres were delivered at fast and slow flow rates to check the linearity of the flow integration. The instrument was checked

periodically during the session for calibration drift. Indoor temperature and relative humidity were recorded at the time of calibration using a digital thermohygrometer (Protimeter Diagnostic Mark III, Protimeter plc, Marlow, U.K.). All spirometric indices were corrected automatically to BTPS.

3.3.3. Impedance Tympanometry

Middle ear pressure, compliance, and the relative gradient of the tympanometric curve (see Appendix C) were measured on both ears using a Microlab "Earscan" configured for impedance measurements (Micro Audiometrics, Port Orange, Florida, U.S.A). This uses a probe tone of 226 Hz at 85 dB and sweeps from +200 to -312 daPa at 100 daPa/sec. Subjects were asked to swallow a sip of water immediately prior to the measurement, to ensure that patent Eustachian tubes would be ventilated. Tympanogram types were defined on the basis of the modified Jerger classification proposed and validated by Fiellau-Nikolajsen (176):

Type	M.E.P. (daPa)	Gradient	Interpretation
A	+200 to -99.9	> 10%	Normal tympanogram
C1	-100 to -199.9	> 10%	Mild underpressure
C2	-200 to -312	> 10%	Severe underpressure
B	No peak	< 10%	Middle ear effusion

3.3.4. Exercise Challenge

Each child ran for six minutes in a corridor or classroom. Verbal encouragement was given to maximize the effort, and the severity of the challenge was assessed by monitoring pulse rate over a 15 second period, commencing 15 seconds after the end of the exercise.

3.3.5. Post-Exercise Spirometry

Spirometry was repeated five and ten minutes after the end of the exercise challenge. On each occasion, three forced expiratory manoeuvres were performed, and the indices recorded from each set of three expirations were determined as above. Two children with symptomatic wheeze at the five minute test were not required to complete the ten minute test. Both of these normally used inhalers and their bronchospasm responded to their usual inhaled beta-2 agonist. No overt wheeze developed later if none had been apparent in the first ten minutes after exercise.

3.3.6. Collection of Saliva

An attempt was made to collect at least 1 ml of saliva from each child by asking them to retain a mouthful of saliva and spit into a plastic cup. The specimen was then decanted into a specimen tube and frozen within

eight hours of collection. Samples were transported in a refrigerated box for cotinine assay by gas-liquid chromatography (72) at the Institute of Psychiatry, London.

3.3.7. Repeat Measurements

Four of the larger schools were revisited at an interval of between one and four weeks to obtain duplicate measurements by spirometry on the same children on different occasions. The test sessions were separated by an interval of between one and four weeks during the months of January to March, and were not necessarily at the same time of day. In the second visit to these schools, further measurements were taken after a five minute interval to assess within-occasion variability of spirometric indices. In the largest school the full protocol including exercise test, tympanometry and saliva collection was repeated on the same children at an interval of ten days.

3.4. Measurements in the Home

3.4.1. Semiquantitative Survey of Bedroom Humidity

All families whose child was eligible for the respiratory examination survey were included in a

screening survey to identify the children's bedrooms with the highest humidity. Each child was given a padded envelope at school, containing a 3" x 1" x 1" ramin wood block, with instructions to their parents to place this in the child's bedroom for a week (Appendix A). Following a reminder circulated on the sixth day, the wood blocks were returned in a self-sealing plastic bag to a collecting box in the classroom. On the eighth and ninth days, the blocks were unwrapped and their moisture content determined by a surveyors electrical conductance meter (Protimeter Diagnostic Mark III, Protimeter plc, Marlow, U.K.). The effective range of this instrument is 9.5% to 20% moisture content, equivalent to ambient relative humidities from 40% to 85% at room temperature.

The screening survey was launched in mid-January 1987, at the start of a week of snowy weather which resulted in the closure of several schools. The cold weather probably accentuated differences between homes in terms of bedroom humidity, but resulted in a poorer response than in the questionnaire survey. Of the 941 children eligible to participate in this part of the survey, 778 (83%) satisfactorily returned a wood block.

3.4.2. Monitoring of Bedroom Temperature and Relative Humidity

During the subsequent four months, an attempt was made to visit the homes of 377 children, comprising all those in eight schools, those in the top quintile of the humidity distribution (as assessed in the wood block survey) and the remainder of the homes reported to be affected by dampness or mould growth. After a period of instruction, these visits were carried out unsupervised by a part-time survey assistant. Measurements were taken in 330 homes, of which 317 were usable in the analysis (84% of the target sample). Technical problems with the instruments, including interference by the child or their siblings, accounted for most of the unusable recordings.

In each home, the temperature and relative humidity of the child's bedroom were monitored for seven days by thermohygrograph (Casella Ltd, London, U.K.). This instrument measures temperature by bimetallic strip and humidity by changes in the length of a treated human hair, and both are charted on a slowly moving drum. The thermohygrographs were installed in a position between 3 and 6 feet high and out of direct sunlight. On completion of the recording, their calibration was checked by a spot measurement of wet and dry bulb

temperature using an aspirated psychrometer. The relative humidity was calculated from the wet and dry bulb thermometer readings using standard formulae (12).

Thermohygrograph charts were sent to the Building Research Establishment, East Kilbride, for computer analysis. The seven-day recordings were digitized and hourly, daily and weekly mean values for temperature and relative humidity were calculated. Vapour pressure, a measure of the actual water content of the air, was derived from temperature and relative humidity using standard formulae (12).

The validity of the ramin block moisture content as an indicator of mean weekly relative humidity was assessed in the homes visited for thermohygrograph measurements. A wood block was placed on top of each thermohygrograph and returned at the end of the week, in a sealed bag, for measurement of moisture content as in the screening survey. The moisture content was then correlated with the mean weekly relative humidity during the period of equilibration in the child's bedroom.

Five homes, representing the range of bedroom humidity levels, were selected within the first two weeks for continuous monitoring over the entire four-month period. The day-to-day within-home variability of bedroom conditions was assessed, and these variations

were related to changes in outdoor climatic conditions, as recorded at Turnhouse Airport by the Metereological Office. In collaboration with Dr Christopher Sanders at the Building Research Establishment, a statistical procedure was developed to adjust the recordings from each home for the climatic conditions during the week of recording. This is discussed in more detail in section 3.5.3.

3.5. Statistical Analysis

3.5.1. General

Questionnaire and clinical survey data were computerized and analyzed using SAS (185). Multiple logistic regression models were fitted using GLIM (186). These models were used in a variety of different analyses, and each is described in more detail in the relevant results section. Extensive use was made of the chi-square (X^2) statistic proposed by Mantel (187) to assess the significance of trends in 2 x k and j x k contingency tables.

3.5.2. Repeatability

The within-subject variability of each spirometric index was investigated by examining the distribution of

differences between pairs of readings obtained from the same subject. The mean of this distribution described the effect of the order of the measurements and the variance of the differences was taken to represent twice the within-subject variance of a single reading.

There are two main components to the variability of measurements taken on different occasions; within-occasion variability (due to effort on the part of the subject and to the tolerance of the instrument) and true biological variation from hour to hour and day to day (due to physiological and pathological factors). In addition, there may be a contribution from changes in the calibration or linearity of the instrument, but the methods employed here attempted to minimize such effects. Longer-term biological changes, including seasonal variations, were not addressed by these short-term repeatability studies.

In many epidemiological field surveys, a single measurement of a given spirometric index is used to rank individuals in the study population. Such measurements are typically taken at varying times of day over a period of weeks or months, so the estimates of between-occasion variability derived here are directly relevant. The power of an index to distinguish between groups or individuals depends not only upon the

variability of the measurement, but also upon the spread of true values among individuals in the population. This is commonly expressed as the coefficient of reliability (188), which is the proportion of the variance of a measurement that is attributable to differences between individuals. The proportion attributable to the variability of the measurement within individuals is one minus the reliability coefficient; this within-subject component includes both measurement error (within occasions) and biological variation (between occasions).

3.5.3. Thermohygrograph Data

Particular problems were raised by the nature of the temperature and relative humidity recordings which were taken during the period January to April 1987, when mean weekly outdoor temperature ranged from -3 to +13 deg C, and mean weekly outdoor vapour pressure from 4 to 11 mb. As indoor temperature and relative humidity vary with outdoor conditions it was necessary to consider how each seven-day recording could be adjusted for climatic variation. Five homes, representing the range of humidity levels encountered in the total sample, were monitored continuously over the four month period. The response of bedroom conditions in these "core" homes was used to derive an adjustment procedure

for the temperature and relative humidity recordings in the remaining homes.

Relative humidity is a function of both vapour pressure (which reflects absolute humidity) and temperature (which determines the saturation vapour pressure at which condensation will occur). The relationship between indoor relative humidity and outdoor conditions is complex, depending upon the respective temperatures and vapour pressures. Thus, in well-heated bedrooms relative humidity was lower in colder weather, reflecting the lower outdoor vapour pressure usually found during the winter. However, in poorly-heated bedrooms the relative humidity was higher during the winter, because it was determined by the indoor temperature which varied to a greater extent with external conditions.

Using daily means from each "core" home, the relationship between indoor and outdoor vapour pressure was close to linear, with a regression coefficient in each home of approximately 0.6, so this coefficient was used in the adjustment procedure. The relationship between daily means for indoor and outdoor temperature for the same homes was more complex. The warmest bedroom was maintained at approximately constant temperature, regardless of weather conditions. On the

other hand, the temperature of the coldest bedroom (which was unheated) was highly sensitive to external temperature. The remaining three bedrooms showed intermediate patterns, depending upon the efficiency of the heating and the temperature threshold at which it was used. The regression lines for indoor upon outdoor temperature in each "core" home were therefore of different slope, but tended to converge at the point corresponding to indoor temperature 22 deg C, outdoor temperature 20 deg C. The adjustment procedure adopted was therefore:

$$VP_A = VP_I + 0.6(9 - VP_O)$$

$$T_A = T_I + \frac{(22 - T_I)}{(20 - T_O)}(10 - T_O)$$

Subscripts A, I and O denote adjusted indoor, measured indoor, and the concurrent outdoor recordings, respectively. Adjusted relative humidity was derived from the adjusted values for vapour pressure and temperature, using standard formulae (12). The constants in the adjustment procedure were chosen to standardize all measurements to outdoor conditions of 10 deg C and 9 mb, which are close to the annual mean temperature and vapour pressure at Turnhouse Airport.

4. RESULTS

4.1. Ventilatory Function

4.1.1. Within-Occasion Variability

Duplicate readings at the same test session were available for 232 children. These included 27 (11.6%) who had a history of wheeze in the past year, of whom eight had wheezed in the past month and four regularly took inhaled therapy for asthma.

There was no substantial order effect for any of the indices; the average differences between the first and second measurements were all less than 2% of the mean value for the corresponding index. For FEV1 the average difference was 0.6%. The within-occasion variability of each index is shown in Table 1, expressed in terms of the standard deviation of a single reading, and the standard deviation divided by the mean value for the corresponding index (coefficient of variation). These figures should be doubled to obtain 95% confidence intervals for each measurement.

In terms of its coefficient of variation, FEV1 was the least variable measurement, closely followed by FVC. Although flow rates during early expiration were more variable in absolute terms, the coefficient of variation was greater for the terminal part of the spirogram (Table 1).

An important application of these estimates of within-occasion variability was to evaluate the effect of chance variations upon changes in spirometric indices during the exercise test for bronchial reactivity. For such purposes, the variability of the measurement was more conveniently expressed on a logarithmic scale, since the outcome in challenge tests is usually the proportional, rather than absolute, change in airflow. The right-hand column of Table 1 shows the standard deviation of the log (base 10) of a single reading. The coefficient of variation on an arithmetic scale is approximately equal to the antilogarithm of this value minus one.

Challenge tests generally require repeated measurements of the same spirometric index at intervals after a fixed challenge, or after increasing doses of a pharmacological agent. At each test random errors of measurement may give rise to a spurious false positive result, even if there has been no true change in ventilatory function. The probability of this occurrence depends upon the cut-off point chosen to define "abnormality", the within-occasion variability of the spirometric index chosen, and the number of comparisons made with the baseline reading. Table 2 illustrates these effects for two commonly used indices.

Although PEFR was the least variable flow index in this age-group, random errors in its measurement were sufficiently large to limit the specificity of any test based upon changes in this index. In contrast, the greater precision of FEV1 suggested that false positive results would be rare, even on repeated comparisons, with abnormality defined as a 20% reduction from baseline, as is commonly applied. The calculations in Table 2 assume no true change in ventilatory function. In practice, the specificity of tests for bronchial reactivity will also depend upon the effect of the challenge upon the function of normal airways.

4.1.2. Between-Occasion Variability

Results of spirometry on two different occasions were available for 171 children who were free of upper respiratory symptoms at each test. These included 20 (11.7%) with a history of wheeze in the past year, of whom six had wheezed in the past month and three regularly took inhaled treatment for asthma.

Table 3 shows the variability of each index between occasions, expressed in a similar manner to Table 1. As expected, the standard deviation for a single reading of each index was greater than the corresponding value for within-occasion variability. The proportion of the between-occasion variance attributable to measurement

errors (as estimated by within-occasion variances from Table 1) is indicated in the right-hand column of Table 3. Measurement errors accounted for approximately half of the between-occasion variance for most of the indices, but for PEFR and FEV1 this component of variation was proportionately smaller.

Table 4 shows the mean and standard deviation of the measured first readings, and the coefficient of reliability for each index, calculated for the 232 children participating in the repeatability study. The most reliable measures were FVC and FEV1, for which within-subject variability accounted for less than one-quarter of the observed variance. Indices of flow during early expiration were more reliable than FEF75% and FEF75-85%, which were derived from the terminal part of the spirogram. For the latter, half of the observed variance was attributable to within-subject variation, and the power to distinguish between individuals was correspondingly weaker. Height and sex accounted for a greater proportion of the variance of FEV1 and FVC than they did for flow rates.

4.1.3. Variability at Different Levels of FEV1

The within-occasion and between-occasion variability of FEV1 was investigated for children within the lowest, middle and highest tertiles of the distribution of

measured FEV1. In the lowest tertile (FEV1 less than 1313 ml) the standard deviation of a single measurement on a given occasion was 64.5 ml, and the standard deviation between occasions was 154.1 ml. The corresponding figures for the middle tertile were 61.0 ml and 90.2 ml. In the highest tertile (FEV1 greater than 1412 ml) the standard deviations were 54.7 ml and 92.9 ml, respectively: Analyzing the standard deviation of each pair of readings there was a weak but statistically highly significant negative correlation with the the mean of each pair ($r = -0.17$ for 232 pairs on the same occasion, $r = -0.21$ for 171 pairs on different occasions). The fact that in absolute terms, both estimates of variability were higher among the children with the lowest readings, implies greater discrepancy in relative measures such as the coefficient of variation.

4.1.4. Relationship to Symptoms

The relationship between pre-exercise spirometry and past and present respiratory symptoms was studied by dividing the study sample into four groups on the basis of their history of lower respiratory disease as reported by parents in the postal questionnaire:

Recent wheeze Children who had wheezed in the past year

Chest colds	Children without recent wheeze who had a tendency for colds to go to the chest in the past year
LRD in past	Children with a history of lower respiratory disease (asthma, wheezing, bronchitis or pneumonia) who were not included in the two categories above
No LRD	Children not included in any of the above categories.

These definitions are hierarchical and mutually exclusive. Thus, one half of the children who were described as having a tendency for colds to go to the chest also had wheezed in the past year, and were included in the recent wheeze group. Similarly, one third of the children with a history of lower respiratory disease, but without recent wheeze, were prone to chest colds, and therefore were included in that group.

Complete data on baseline spirometry and medical history was available for 880 children (98% of those eligible for testing, 99% of those actually tested). The prevalence of recent wheeze, chest colds and past lower respiratory disease among this group (as defined above) were 13.0%, 9.4% and 6.9%, respectively. The corresponding prevalences among the children whose

parents responded to the questionnaire, but did not consent to spirometric tests, were 8.7%, 9.5%, and 5.5%, respectively.

Baseline spirometry was adjusted in a multiple regression model for standing height, sex, time of day and outside temperature and relative humidity, each of which was significantly related to at least one index of ventilatory function. In a further model, the effect of recent symptoms and housing tenure were also included.

Recent symptoms were reported by the child at the time of the test, and were defined as cough, wheeze, sore throat, or running nose during the week before the test. Their effect (independent of disease history) was most marked for indices of flow early in expiration, and was significant ($p < 0.05$) for peak expiratory flow rate (2.7% reduction) and FEF25% (4.5% reduction). Recent symptoms had little influence upon end-expiratory flow rates. The reductions in FEV1 and FVC were small and non-significant (0.7% and 0.9%, respectively).

Housing tenure was included as a broad indicator of social background and home conditions which could potentially confound the relationship between disease history and ventilatory function. After adjustment for

height, all spirometric indices were lower in the children from rented, as compared with owner-occupied homes and the proportion in each lower respiratory disease group was higher in the rented homes. The prevalences of recent wheeze, chest colds and past lower respiratory disease among children from owner-occupied homes were 10.7%, 7.0% and 5.8%, respectively. The corresponding figures for rented homes were 16.6%, 15.2% and 8.6%.

Table 5 shows the adjusted spirometric indices for the four disease groups. With the exception of forced vital capacity among children with past disease, all indices were reduced among the children with past or present lower respiratory complaints. The reductions were generally greatest in the group with wheeze in the past year, even after controlling for recent symptoms. The unexpected exception here was peak expiratory flow rate. In all disease groups, the indices showing the greatest reduction in relative terms were those measuring flow during mid-expiration (FEF25-75% and FEF50%). Exclusion of recent symptoms and housing tenure from the model made little difference to these results.

A clearer pattern emerged when volumes and flow rates were expressed as a percentage of forced vital capacity

(Table 6). Again the mid-expiratory flow rates were most affected in each group. This was the only significant difference for the non-wheezy children with chest colds. In contrast, children with recent wheeze had markedly lower values for all ratios, except for peak expiratory flow rate. Statistically significant decreases in all ratios were found among the children with a past history of lower respiratory disease, and these were of a comparable magnitude to those among children with wheeze in the past year.

4.2. Exercise-Induced Bronchial Lability

4.2.1. Distribution

The exercise test was completed by 881 children (99% of the 892 tested). This figure includes five children who were tested on oral treatment with theophyllines or steroids and six who regularly used steroid inhalers. Nine children did not complete the exercise challenge, and two were unable to record a satisfactory pre-exercise spirogram. The distribution of bronchial lability, as measured by the reduction in FEV1 occurring after exercise, is shown in Figure 1. The lower part of the figure shows the distribution of changes in FEV1 that would be expected by chance alone,

assuming no true effect of exercise on ventilatory function. The expected distribution was derived from within-subject within-occasion repeatability estimates from 232 children in the same population (section 4.1.1.). The mode of both distributions is less than zero because the minimum of two post-exercise readings was used to define the FEV1 after exercise. This approach was used throughout the analysis because the time course of post-exercise bronchospasm was uncertain and appeared, in the data, to vary from subject to subject.

The observed distribution of lability differed from that expected by chance alone, principally due to the presence of extreme reductions in FEV1. This "abnormal" tail merged imperceptibly with the bulk of the measurements, and there was no evidence of a bimodal distribution. Reductions in FEV1 by greater than 20% of the baseline level were estimated to occur by chance alone once in one thousand tests, whereas 40 children (4.6%) were observed with this degree of post-exercise bronchospasm. There were also rather more large increases in FEV1 than would have been expected by chance alone. These may be due to a learning effect among a few children with spuriously low initial values. The modes of the observed and expected distributions were similar, suggesting that in the

majority of children, the exercise challenge had little effect on FEV1 measured five or ten minutes later.

Overall, 113 children had a history of wheeze in the past year, and 56 (50%) of these had used an inhaler during the same period. Among the eleven children tested while on long-term treatment, three experienced a reduction in FEV1 of greater than 20% after exercise; in another three the reduction was between 10% and 20%. None of this group showed an increase in FEV1 after exercise. Although it seems likely that, in the absence of treatment, all these children would have experienced abnormal exercise-induced bronchospasm, their results have been presented separately throughout. Fifteen children had used cromoglycate or beta-2 sympathomimetic inhalers only during the 24 hours before the test. All of these were tested at least six hours after their last dose, and their results have been included in the general distribution. A further thirty children gave a history of inhaler use in the past year. The prevalence of abnormal lability was similar among those who had and had not used their inhaler in the past 24 hours; five (33%) of the former group and ten (33%) of the latter experienced a reduction in FEV1 of more than 20%.

The variation between subjects in their response to the exercise challenge was independent of height (correlation coefficient r = 0.03), time of day (r = 0.04), outside temperature (r = 0.03), outside relative humidity (r = -0.02), indoor temperature (r = 0.06) and indoor relative humidity (r = 0.04). The mean pulse rate, measured between 15 and 30 seconds after the exercise challenge, was 155 beats per minute. As pulse rates are known to fall rapidly on cessation of exercise in children (161), pulse rates during the test were probably 15-20 beats per minute higher. This relatively crude index of the severity of the challenge was not correlated with exercise-induced bronchospasm (r = 0.004). The reductions in FEV1 were somewhat greater in boys, but the mean difference was small (0.5% of baseline FEV1) and not statistically significant (p = 0.21).

4.2.2. Relationship to Symptoms

Table 7 shows the relationship of exercise-induced bronchospasm to history of asthmatic symptoms, as obtained from parents in the postal questionnaire survey. As expected, abnormal lability was more common among the children with a history of recent wheeze, particularly those with wheeze in the past month. However, only half of the children with unequivocal

exercise-induced bronchospasm (more than 20% reduction in FEV1) had wheezed in the past year. In the questionnaire, two thirds of the wheezy children were reported to suffer wheezing or shortness of breath after exercise. These reports did not predict measured exercise-induced bronchospasm any better than parental responses to more general questions about recent wheeze.

The distribution of bronchial lability among children with a history of wheeze in the past, but not in the previous year, differed little from those who had never wheezed (X^2 7.93, 5 df, $p > 0.10$). Among the children who had never wheezed, there were 33 with a history of bronchitis or pneumonia. Only two (6%) of these experienced a reduction in FEV1 greater than 10%.

Sixty-three (56%) of the children with wheeze in the past year had been diagnosed asthmatic, and 53 (84%) of these had used an inhaler in the past year. In contrast, only three (6%) of the remaining fifty children with wheeze in the past year had received inhaled bronchodilator therapy. Table 5 shows that the children labelled asthmatic had somewhat more severe bronchospasm after exercise than those whose wheezing had not been attributed to asthma, but there was considerable overlap between the two distributions. The

greater lability in the asthmatics was partly, but not wholly, explained by the higher frequency of wheezing attacks in this group. The prevalence of wheeze in the past month was 38% among the 63 asthmatic children, compared to 24% among the 50 children with wheeze not labelled as asthma.

The relationship between bronchial lability and other symptoms associated with asthma was analyzed among the children with and without wheeze in the past year (Table 8). Complete questionnaire information was available for 758 non-wheezy children and 101 wheezy children (excluding those tested on treatment). As expected, the prevalence of each symptom was substantially greater among the wheezy children. The prevalences of both nocturnal and daytime cough increased with the degree of exercise-induced bronchospasm among wheezy children. Among the non-wheezy children, the prevalence of each symptom was highest among the small number of children whose FEV1 was reduced by more than 20%. This was largely attributable to three children in this group who suffered from multiple symptoms. There was no association between a tendency to chesty colds and bronchial lability among the children with no recent wheeze.

The relationship between asthmatic symptoms and exercise-induced bronchial lability was explored further by multiple logistic regression analysis. These models included exercise-induced reduction in FEV1 as a continuous explanatory variable, and wheeze in the past year as a dichotomous control variable. The outcome variables were those included in Table 8. Before adjustment for recent wheeze, lability was significantly related to nocturnal cough (X^2 8.34, 1 df), daytime cough (X^2 5.65, 1 df), and chest colds (X^2 10.9, 1 df), but not to school absence due to chest trouble (X^2 2.56, 1 df). After adjustment these associations were no longer significant, although they remained in the expected direction (X^2 2.64, X^2 0.70, X^2 0.12, X^2 0.09, respectively, all on 1 df).

4.2.3. Social Class Distribution

Further evidence of the different epidemiological characteristics of wheeze and other symptoms often attributed to asthma was provided by their different social class distributions (Table 9). Both recurrent night cough and chesty colds were strongly related to parental social class, with higher prevalence in the children of manual workers and parents of unknown social class. In contrast, neither wheeze nor diagnosed asthma were significantly related to social class, but

there was some evidence of a mismatch between morbidity and diagnosis among poorer families. Although there was a higher prevalence of wheeze in classes IV and V, there was a lower prevalence of diagnosed asthma, with a correspondingly low rate of inhaler use.

Exercise-induced bronchospasm showed no trend with social class (Table 9). Although mean post-exercise pulse rate was slightly higher in children from social classes I and II (156 per minute) than classes IV and V (153 per minute), there was no overall effect of pulse rate on the response to exercise (section 4.2.1.), so that differences in the degree of challenge to the airways are unlikely to have influenced the social class comparisons of bronchial lability.

4.3. Impedance Tympanometry

4.3.1 Distribution and Prevalence of Abnormality

A total of 1721 tympanograms were obtained from 872 children (98% of those tested). In 23 children, satisfactory results were obtained from one ear only, but tympanograms were available for both ears of 849 children (95% of those tested). The distributions of middle ear pressure, relative gradient and peak compliance among the 1721 tympanograms are shown in

Tables 10 to 12. Compliance showed a skewed but continuous distribution. Among those tympanograms with a defined peak, there was a suggestion of bimodality in the distribution of middle ear pressure, with a trough in the region -250 to -200 daPa.

Overall, 108 (6.3%) tympanograms met the criteria chosen to define middle ear effusion (Table 10). In terms of relative gradient, there was a clear distinction between these results and the remainder of the distribution; no tympanograms were recorded with relative gradient between 1% and 10%, and only four between 10% and 15%. Unexpectedly, among the 1613 ears without effusion, there was almost no correlation between middle ear pressure and gradient ($r = 0.07$) (Table 10). The correlation between pressure and peak compliance was similarly weak ($r = 0.05$) (Table 11), but there was a stronger correlation between compliance and relative gradient ($r = 0.53$). Although the latter was in the expected direction, with lower peak compliance associated with lower gradient, combinations of low compliance and above-average gradient were not uncommon (Table 12). Thus, there appeared to be little evidence of a progression from tall steeply peaked "normal" curves through flatter, less steeply peaked curves. This accentuated the qualitative distinction between tympanograms with and without a definable peak.

Table 13 shows the relationship between the pressures in each ear among the 849 children with bilateral tympanograms. About half of those with an effusion in one ear had an effusion in the other, the prevalence of bilateral effusions being 3%. Middle ear pressures in the two ears were highly correlated ($r = 0.65$), as were the relative gradients ($r = 0.48$) and peak compliances ($r = 0.59$). In view of these correlations, the tympanogram from the more abnormal ear was used to characterize the degree of abnormality in each child. This allowed the results of the 23 children with unilateral tympanometry to be included in aetiological analyses.

4.3.2. Repeatability

Tympanometry was repeated within fifteen minutes in 82 children (161 ears). Two ears met the criteria for effusion on both tympanograms. In a further two ears with effusion on one recording, the middle ear pressure on the other tympanogram was determinate, but in both cases was less than -280 daPa, with relative gradient less than 20%. Among the remaining 157 ears, there was a negligible order effect in pressure measurements, with a mean difference of 2.5 daPa between first and second readings. The order effects for compliance and

relative gradient were also small, the mean differences being 0.034 ml and 0.45%, respectively.

The within-subject standard deviation of middle ear pressure on the same occasion was 22 daPa, corresponding to a reliability coefficient of approximately 0.95. The equivalent figures for compliance were 0.13 ml (reliability 0.89) and for relative gradient were 7.1% (reliability 0.60). However, for relative gradient, within-subject variation within the range 20% to 80% may be of little clinical relevance, if the fundamental distinction is considered to be between gradients close to zero (indicating effusion) and the remainder of the distribution.

Tympanometry was repeated at an interval of ten to fifteen days in 58 children (116 ears). Nine ears met the criteria for effusion on at least one occasion, but only three of these had effusion on both tympanograms. Of the other six ears, the middle ear pressure was less than -200 daPa on the second occasion in two, and greater than -100 daPa in three.

Among the 107 ears free of effusion on both occasions, the within-subject standard deviation of middle ear pressure was 59 daPa, corresponding to a reliability coefficient of 0.66. The equivalent figures for

compliance were 0.21 ml (reliability 0.69) and for relative gradient were 8.5% (reliability 0.41).

4.3.3. Relationship to Symptoms

At the time of examination, each child was asked whether they had experienced cough, runny nose, or sore throat during the previous seven days. Compared with the 474 children without recent symptoms, the 398 who gave such a history had lower middle ear pressure and were more likely to have an effusion (Table 14).

The tympanometric findings in the more abnormal ear were also analyzed against the history of upper and lower respiratory symptoms obtained from parents in the postal questionnaire survey. No association was found between effusion, middle ear pressure or relative gradient and any of the following symptoms as reported in November, two to six months prior to examination: blocked or runny nose (past month), daytime cough (past month), nocturnal cough (past month), wheeze (past year), chesty colds (past year) and hayfever (past year). The prevalence of effusion was lower among the 89 children with hayfever than among the remainder (5.6% v 9.7%, X^2 1.11, 1df), although it was higher among the 113 children with wheeze (12.4% v 8.9%, X^2 1.03, 1df).

Both middle ear underpressure and effusion were strongly associated with pain or discharge in the ear (past year) and a history of tonsillectomy or adenoidectomy (ever) (Table 14). The prevalence of middle ear effusion was significantly more common among the 450 children with a history of sore throat in the past year (11.8% v 7.0%, X^2 5.11, 1df), although this symptom was not clearly related to underpressure. The excess of middle ear effusion among children with a history of ear trouble was significant (X^2 9.77, 1df) and the association of effusion with tonsillectomy or adenoidectomy was even more striking (X^2 21.0, 1df) (Table 14).

4.4. Respiratory Disease and the Home Environment

4.4.1. Questionnaire Data

The parents of 1095 children received a questionnaire, and usable replies were obtained for 1012 (92%). Information relating to respiratory symptoms and housing conditions was available for between 926 (85%) and 1004 (92%), depending upon the detail required. Complete information relating to dampness, mould growth, wheeze and exercise-induced bronchial lability was available for 873 children (80% of the original

sample, 97% of those eligible for testing). The prevalences of wheeze in the past year (12.7%) and exposure to mould in the home (9.3%) were somewhat higher in this group than among those with incomplete information (10.0% and 6.3%, respectively).

The relationships between "lower" respiratory symptoms and various aspects of the home environment are shown in Table 15. The prevalences of wheeze and chesty colds were greater, by a factor of between two and three, among the children from homes reported to be affected by damp patches on walls, or by mould growth, particularly when their bedroom was affected. Cough at night and during the daytime was significantly more common among children from damp bedrooms, and a smaller non-significant excess was observed in children from mouldy bedrooms. Both night cough and chesty colds were influenced by crowding and the presence of smokers in the household. There was little evidence that domestic fuels were important. Paradoxically, chesty colds were significantly less common in households using gas for cooking, but more prevalent in the small number of children exposed to unvented gas heating appliances. These relationships in part reflected differences in the use of fuels by owner-occupiers and tenants of rented housing.

Table 16 shows equivalent information for "upper" respiratory symptoms. Significant associations were found between frequent trouble with a blocked or running nose and mould growth in the bedroom, which was of a similar magnitude to that seen for "lower" respiratory symptoms. The pattern of association between dampness and hayfever was inconsistent; when all damp homes were considered together, the difference from the prevalence in unaffected homes was negligible (X^2 0.54, 1df).

The association between damp, mouldy housing and wheeze was remarkable in view of the lack of variation of wheeze with other environmental factors in the home. Compared to rented homes, owner-occupied homes were less likely to be affected by dampness (8% v 30%) or mould growth (5% v 19%), and this accounted for the difference in the prevalence of wheeze by housing tenure. Among homes unaffected by damp or mould, the prevalence of wheeze was similar in the rented sector (11.1%) and in owner-occupied homes (10.6%). By contrast, chesty colds, night cough, daytime cough and running nose were influenced by housing density and number of smokers in the household, factors which were strongly related to tenure and which were, therefore, potential confounders for the relationship with dampness or mould growth (Tables 15 and 16).

Possible confounding effects were investigated further by multiple logistic regression models with wheeze (in the past year) as the outcome variable. The unadjusted odds ratio for mould anywhere in the home was 3.70 (95% confidence interval 2.22-6.15, X^2 27.7, 1df). In a model including housing tenure, number of smokers in the household, persons per room and gas cooking, the odds ratio for mould was 3.00 (1.72-5.25, X^2 15.2, 1df). The effect of mould was independent of housing tenure (X^2 for interaction term 0.41, 1df). There was a close correlation between damp walls and mould growth; 48% of the homes affected by dampness were reported to be mouldy, and 80% of the mouldy homes were reported to be damp. In terms of its effect upon wheeze, mould appeared to be the more important variable. In a model including damp walls (anywhere in the house), the effect of mould remained significant (X^2 7.52, 1df), whereas the effect of dampness independent of mould growth was negligible (X^2 0.60, 1df).

The relationships between housing conditions and chest colds, night cough, daytime cough and nasal discharge were investigated in similar multiple logistic regression models, using each respiratory symptom in turn as the outcome variable. The association between mould and chest colds was independent of housing tenure, persons per room, number of smokers and gas

cooking (odds ratio 2.08, 1.22-3.51, X^2 7.26, 1df). Inclusion of wheeze (in the past year) as a further explanatory variable reduced this effect and it was no longer significant, although it remained in the same direction (odds ratio 1.43, 0.77-2.70). At least part of the association between chesty colds and mould appeared, therefore, to be a consequence of a recent wheezing tendency.

The weaker associations of night cough and daytime cough with mould in the home were entirely explained by their common association with rented housing. Adjusting for tenure, the odds ratios for night cough and daytime cough associated with mould were 0.92 and 0.95, respectively. The effect of mould upon nasal discharge, after adjustment for tenure, remained in the expected direction but was non-significant (odds ratio 1.61, 0.89-2.90, X^2 2.42, 1df). Further adjustment for the effects of housing density, number of smokers and gas cooking made little difference to these results.

4.4.2. Mould, Wheeze and Bronchial Lability

Objective evidence of airways reactivity was collected to investigate the possible contribution of reporting bias to the observed association between wheeze and mould in this and previous questionnaire data. As expected, wheeze during the past year was more

prevalent among the children with demonstrable exercise-induced bronchospasm. If no reporting bias had existed, this relationship should have been independent of housing conditions. In fact, for any given degree of bronchial lability, a parental report of wheezing was more frequently obtained for children from mouldy homes (Table 17). In a logistic regression model with wheeze (in the past year) as the outcome, bronchial lability was included as a continuous explanatory variable. Its relationship to wheeze was approximately linear (X^2 for quadratic term 1.05, 1df), and was modelled as such. The effect of mould in the home was independent of lability (odds ratio 3.50, 1.95-6.47, X^2 16.1, 1df), and constant across the range of lability observed (X^2 for interaction term 0.10, 1df).

The higher prevalence of reported wheeze among children from mouldy homes, for any given degree of demonstrable airways reactivity, suggested that reporting bias explained a substantial part of the association between wheeze and damp or mouldy housing. However, demonstrable exercise-induced bronchospasm was more common among the children from mouldy homes, and a higher proportion of this group were receiving inhaled steroid or oral therapy for asthma. This point will be explored in more depth in sections 4.4.6. and 4.4.7.

4.4.3. Measurements of Indoor Temperature and Relative Humidity

The number of children included in the semiquantitative survey of bedroom humidity was 941 (86% of the original sample), and, of these, 778 (83%) satisfactorily returned a ramin block. The prevalence of symptoms and housing characteristics were found to be similar among those who did and did not complete this stage of the survey. Snowy conditions resulted in the closure of a few schools, contributing to the incomplete response at this stage, but, advantageously, the cold weather probably accentuated differences between well-heated and poorly-heated bedrooms in respect of ambient relative humidity. During the week of the wood block survey, mean outdoor temperature was +1 deg C and mean vapour pressure 5.6 mb. Moisture content varied from less than 9% (the limit of detection of the instrument) to 20%, equivalent to a range of relative humidity from less than 45% to over 80%. The distribution was skewed to the right, with a long upper tail, mainly from rented housing. The upper quintile of moisture content consisted of values above 13% (equivalent to approximately 65% mean relative humidity).

During the subsequent four months, an attempt was made to visit the bedrooms of 377 children, and usable

recordings of both temperature and relative humidity were obtained for 317 (84%) of the subsample (156 owner-occupied and 161 rented homes). Mean weekly temperatures as recorded ranged from 5.8 to 22.9 deg C; after adjustment for climatic variation the distribution was approximately normal with mean 17.8 deg C and standard deviation 1.8 deg C. Mean weekly relative humidity as recorded ranged from 28% to 77%; after adjustment the distribution was approximately normal with mean 53% and standard deviation 6.5%.

Data from the five homes which were monitored continuously for four months was used to validate the statistical adjustment for climatic variation. An ideal adjustment procedure would yield adjusted indoor conditions which remained constant for each home, regardless of climatic variation. Following the adjustment procedure adopted, there remained a weak correlation between weekly means for adjusted indoor temperature and outdoor temperature ($r = +0.27$), between adjusted indoor relative humidity and outdoor temperature ($r = -0.22$), and between adjusted relative humidity and outdoor vapour pressure ($r = -0.15$). Pooled estimates of the within-home variability of adjusted weekly means for temperature, vapour pressure and relative humidity, expressed as a coefficient of variation, were 4.2%, 7.6% and 6.0% respectively.

The estimation of bedroom relative humidity in the wood block survey was simultaneous and therefore free of many of the assumptions implicit in this adjustment procedure. The precision of moisture content as a measure of relative humidity was assessed by placing a wood block beside each thermohygrograph during the thermohygrograph survey. Comparison of wood block moisture content with weekly mean relative humidity suggested that the coefficient of variation for a humidity estimate based on moisture content would be approximately 10% in the range 50% to 70% relative humidity. However, any comparison of homes based on a single week's measurement implies that the ranking of homes over a longer period of time remains relatively stable, and it is probable that the true precision of the measurement is lower than these figures suggest.

The relationships between the adjusted weekly means for temperature and relative humidity and various characteristics of the child's bedroom, as reported in the questionnaire, are shown in Table 18. Multiple regression modelling, with a stepdown approach, was used to determine the extent to which adjusted temperature and relative humidity could be predicted by questionnaire information. A model including day heat, night heat, open window, and condensation on windows accounted for 14.6% of the variance in adjusted mean

weekly temperature. Inclusion of tenure as a further predictor improved the model slightly, then explaining 16.4% of the variance. For adjusted relative humidity, the significant predictors were: children sharing the room, daytime heat, and dampness on walls. However, together these accounted for only 10% of the variance in adjusted relative humidity. By comparison, moisture content as measured in the wood block survey accounted for 24% of the variance. Although the 37 bedrooms reported to be damp were, on average, more humid, only 17 were in the top quartile of adjusted relative humidity; 9 were below the median of this distribution.

4.4.4. Respiratory Symptoms, Bedroom Temperature and Humidity

Table 19 shows the prevalence of each symptom by quintiles of relative humidity, as assessed semi-quantitatively by wood block moisture content. Although this was a relatively imprecise surrogate measure of bedroom conditions, it permitted the simultaneous ranking of the humidity in a large number of homes, free from the assumptions implicit in the adjustment of thermohygrograph recordings. No symptom had a significant positive relationship with moisture content, nor was there clear evidence of an increase in prevalence in the top quintile. For hayfever, there was

an inverse association which reached significance at the 5% level, but in view of the multiple comparisons being made, this significance test should be interpreted with caution.

Table 20 expresses the relationship between the same symptoms and the thermohygrograph recordings, in terms of the mean adjusted temperature and relative humidity values for the bedrooms of children with and without each symptom. The differences in bedroom conditions between symptomatic and asymptomatic groups were small and, in every case, failed to reach conventional levels of statistical significance.

4.4.5. Baseline Spirometry and the Home Environment

The relationship between baseline spirometric indices and housing conditions, as reported in the postal questionnaire, was studied in 834 children with complete clinical and questionnaire data. Least-squares multiple regression models were used to explore the independent effects of fourteen characteristics of the home environment for each spirometric index, adjusting for sex, height, and test conditions (time of day, outdoor temperature and relative humidity) in each model. The housing factors considered were tenure, number of persons per room, number of smokers in the household, use of gas for cooking, use of a coal fire,

bottled gas appliance, paraffin heater, wood stove, presence in any room of damp patches on walls, patches of mould or fungus, and the following characteristics of the child's bedroom during the winter months: number of children sleeping in the room, heat at night, heat during the day, and window left open at night.

Preliminary investigation of the proportion of variance explained by each model showed that sex, height and test conditions accounted for most of the "explained" variance for each spirometric index (Table 21). The combined contribution of the housing variables considered was small, and four (tenure, persons per room, gas cooking and damp patches on walls) accounted for much of the overall effect due to housing. For each spirometric index, the optimal model (as defined by Mallows' Cp (189)) comprised some combination of these four factors. Further analysis was therefore restricted to a model including these four features of the home environment. Although the number of smokers in the home was not an important determinant of ventilatory function, it has been included for comparison with similar analyses using the salivary cotinine data (section 4.5.2.).

Table 22 shows the independent effects of tenure, density, cooking fuel, dampness and parental smoking on

each spirometric index. Confidence intervals for each effect can be derived from the associated t statistics. With the exception of number of smokers, the independent effects of each housing factor are in the expected direction, with lower volumes and flow rates among children from rented housing, crowded households, families using gas for cooking, and homes with damp patches on walls. With the large number of intercorrelated outcomes and explanatory variables considered, the significance of individual comparisons should be interpreted with caution. More striking is the absence of a consistent or substantial effect for any of the housing factors, including tenure, which may be a more general indicator of family lifestyle.

Table 23 presents similar information for spirometric ratios. When examined in this way, the effect of dampness was more consistent, and was most marked for ratios involving mid-expiratory flow rates. The only measure of ventilatory function affected to any extent by the number of smokers in the household was the ratio FEF75%/FEF50%.

4.4.6. Exercise-Induced Bronchial Lability and the Home Environment

The effect of the same fourteen housing factors on exercise-induced reduction in FEV1 was studied in a

rather different manner, because the distribution of this characteristic was highly skewed, with only a small proportion of clinically significant results. Thus, even after transformation, differences between mean values might be unduly influenced by small effects in the majority of children, at levels of lability that were of little or no relevance to aetiological enquiry. Sex, height and conditions of the test (including post-exercise pulse rate) accounted for little of the variance in bronchial lability so comparisons were not adjusted for these factors. Although the results from the eleven children tested on treatment with inhaled steroids or oral bronchodilator therapy are presented separately, six of these children actually experienced a reduction in FEV1 of more than 10%. None of the remaining five had an increase in FEV1 after exercise, and it seems reasonable to suppose that, in the absence of treatment, all would have experienced a reduction of greater than 10% of baseline FEV1. Comparisons between groups exposed and unexposed to each housing factor were therefore based upon a cut-off at 10% of baseline FEV1, and the eleven children tested on inhalers were included in the "abnormal" group.

881 children completed the exercise test, and related questionnaire information was available for between 840 and 877, depending upon the item required. Table 24

presents the distribution of measured bronchospasm by the fourteen housing variables. There was a higher prevalence of abnormal lability in damp and mouldy homes. The difference in prevalence between homes affected by dampness (19.7%) and those unaffected (12.9%) was of borderline significance (X^2 3.72, 1 df). When the room affected by dampness was considered, the prevalence of abnormal lability was similar among children from homes where the child's bedroom was affected (20.8%, 11/53) and those where only another room was damp (19.0%, 15/79). A similar analysis for mould growth, however, revealed a higher prevalence of abnormality among the children sleeping in mouldy bedrooms (27.0%, 10/37) than those in homes affected by mould in another room (15.6%, 7/45) or unaffected by mould (13.4%, 106/792). When interpreted as a dose-response relationship, this trend was statistically significant (X^2 trend 4.91, 1 df).

The excesses of reactive children in homes using bottled gas or wood stoves were based on small numbers, and could easily have arisen by chance. The effects of housing tenure, crowding, parental smoking and gas cooking were weak and therefore unlikely to be confounding the relationships with dampness or mould growth.

4.4.7 Baseline Spirometry, Bronchial Lability and Bedroom Conditions

The associations of both baseline spirometry and exercise-induced bronchospasm with dampness suggested that indoor temperature and relative humidity might be determinants of these indices of ventilatory function. These relationships were explored further for the 317 children whose bedrooms were monitored in the thermohygrograph survey. None of the spirometric indices or ratios considered in Table 22 and 23 were significantly related to adjusted bedroom temperature or relative humidity, after controlling for sex, height, test conditions and housing tenure. The ratios FEF25-75%/FVC and FEF50%/FVC, which were inversely related to reported dampness, were actually higher in the more humid bedrooms, but these effects of adjusted relative humidity could easily have arisen by chance ($t = 1.20$, 308 df for FEF25-75%/FVC, $t = 0.93$ for FEF50%/FVC). The same indices were lower in the colder bedrooms, but the effect of temperature independent of tenure and humidity was small and non-significant ($t = -0.82$ and $t = -0.70$, respectively).

A satisfactory exercise test was completed by 314 of the 317 children whose homes were monitored. The remaining three children were tested on treatment (one

on oral theophyllines, two on inhaled steroids). These three were included together with children showing a reduction of more than 10% of baseline FEV1 in the "abnormal lability" group. The prevalence of such abnormality was 14% (45/317). Mean adjusted bedroom temperature was 17.77 deg C among the children with abnormal lability, and 17.82 deg C among the remainder (t = -0.03, 316 df). Corresponding mean adjusted relative humidity levels were 52.9% and 52.8% (t = 0.05, 316 df). The correlations between exercise-induced reduction in FEV1 (as a continuous variable) and bedroom conditions were similarly weak; r = -0.02 for temperature, and r = -0.09 for relative humidity.

4.4.8. Impedance Tympanometry, Social Class and Housing Conditions

Tympanometric data for the more abnormal ear of 872 children were related to sex, social class and housing, as reported in the postal questionnaire (Table 25). Overall, middle ear pressure did not vary substantially between males and females, but the prevalence of middle ear effusion was somewhat higher in girls, this difference being of borderline significance (X^2 3.03, 1 df). There was little overall trend in pressure with parental social class. The prevalence of effusion was lowest among children in classes I, II and IV/V, but in

these groups a higher proportion of children had tympanometric evidence of markedly reduced middle ear pressure.

These tympanometric findings may be compared to the sex and social class distribution of recent ear disease as reported by parents in the postal questionnaire. Overall, 24% of children were reported to have had pain or discharge in the ear during the past twelve months. This proportion differed little between boys (22.5%) and girls (25.7%), but there was considerable variation with parental social class. Among children from classes I and II, the prevalence of recent ear trouble was 29.3%, compared with 25.4% in class IIIN, 22.6% in class IIIM, 18.0% in classes IV and V, and 13.9% in households with no employed wage-earner.

The proportion of children reported to have had their tonsils or adenoids removed was 12%. Boys were somewhat more likely to have such a history than girls (13.6% v 11.2%). The proportions in each social class with a history of tonsillectomy or adenoidectomy varied substantially, although the trend was less consistent than that seen for ear trouble. Among children from classes I and II, the figure was 11.7%, compared with 18.3% in class IIIN, 13.0% in class IIIM, 6.4% in

classes IV and V, and 9.2% in households with no employed wage-earner.

The relationship of tympanometric findings to housing conditions is shown in Table 25. Middle ear pressure was lower among children from rented homes and smoking families. There was a trend towards lower pressures in children from damp homes. Crowding, domestic fuels and mould growth appeared to have little effect upon middle ear pressure in the absence of effusion.

Type B tympanograms were more common in all the "exposed" categories (Table 25). The most marked difference was between homes without smokers and those in which two or more adults smoked cigarettes (X^2 4.06, 1 df). Overall, the trend of increasing prevalence with increasing number of smokers in the household was significant (X^2 4.15, 1 df). The prevalence of effusion was somewhat greater in the homes with gas cooking (X^2 2.81, 1 df) or damp patches on walls (X^2 3.01, 1 df). The difference between owned and rented homes was less marked, and non-significant (X^2 1.95, 1 df). However, the prevalence of parental smoking (particularly both parents smoking) was much higher in rented homes, and housing tenure was therefore considered to be a potential confounder for the relationship between passive smoking and middle ear effusion.

The effect of passive smoking was investigated further by multiple logistic regression analysis, using middle ear effusion as the outcome variable. Housing tenure, gas cooking and dampness were treated as dichotomous explanatory variables, and the number of smokers in the household was included as a factor with three levels: none, one, two or more. The independent effect of one smoker in the household (compared to none) was negligible (odds ratio 1.004, 95% confidence interval 0.56-1.78). The effect of two or more smokers remained substantial, although of borderline significance when compared to non-smoking households (odds ratio 1.80, 0.96-3.40). The odds ratio estimates for rented housing, gas cooking and dampness in this model were 1.38 (0.73-2.59), 1.28 (0.73-2.21) and 1.05 (0.70-1.57), respectively.

In contrast to the effect of passive smoke exposure on the prevalence of middle ear effusion, the prevalence of pain or discharge in the ear over the past year differed little between non-smoking homes (23.5%), homes with one smoker (25.3%) and homes with two or more smokers (24.4%). The corresponding proportions of children reported to have had tonsils or adenoids removed were 11.6%, 14.0% and 12.1%. Despite their clear differences between social classes, the prevalences of recent ear trouble and tonsillectomy or

adenoidectomy varied little with respect to housing tenure, the use of gas for cooking, or the presence of dampness in the home.

The effect of the indoor environment was explored in more detail among the 307 children with tympanometric data whose homes had been visited in the thermohygrograph survey. Table 26 shows the mean temperature and relative humidity, adjusted for climatic variation, in groups defined by tympanogram type. There was little overall heterogeneity, and no evidence of a significant trend in bedroom temperature or humidity with degree of tympanometric abnormality. Further adjustment for housing tenure and the number of smokers in the household made little difference to these results (Table 26).

4.5. Respiratory Morbidity and Salivary Cotinine

4.5.1. Distribution of Cotinine Levels

The results of salivary cotinine assay were available for 770 children, 405 from non-smoking households, 241 from homes with one smoker and 124 from homes with two or more smokers. Table 27 shows the frequency distribution of children by numbers of smokers in the

household and quintiles of salivary cotinine concentration.

Almost three-quarters of the children from non-smoking households had detectable cotinine in their saliva, and 10% of this group had levels in the upper two-fifths of the distribution (the maximum being 6.5 ng/ml). The spread of cotinine levels in the children from households containing one or more smokers was broader, and cotinine was detectable in the saliva of all but one of the children from these groups. Six children, five of them from homes with only one smoker, had levels in excess of 15 ng/ml, usually taken as a cut-off point to distinguish smoking and non-smoking adults. These values were 16.5, 17.1, 18.7, 21.0, 25.5, and 36.1 ng/ml.

Table 28 shows the relationship between cotinine levels, sex and housing tenure, within groups with similar numbers of smokers in the home. In view of the skewed nature of the distributions for cotinine, geometric means are presented, with undetectable levels treated as 0.05 ng/ml. Female sex and rented housing were independently and consistently associated with higher cotinine levels, given the number of smokers in the household. These effects were apparent even in non-smoking households.

4.5.2. Respiratory Symptoms, Spirometry and Salivary Cotinine

The relationship between salivary cotinine and disease indices was first studied by grouping the cotinine levels into quintiles. Salivary cotinine was then analyzed as a continuous variable. A logarithmic transformation of the cotinine concentration generally provided a better fit, and for uniformity this has been used throughout. Regression coefficients (for spirometric indices) and odds ratios (for symptoms) are therefore presented per doubling of the cotinine concentration. In view of the effects of sex and housing tenure upon both cotinine levels and most respiratory outcomes, results are presented after adjustment for these factors.

Table 29 shows the relationship between respiratory symptoms and salivary cotinine. Most respiratory symptoms increased in prevalence with increasing salivary cotinine concentration, but after adjustment for sex and housing tenure, only a tendency for colds to go to the chest was significantly associated with log cotinine.

Table 30 shows mean values of selected spirometric indices by quintiles of salivary cotinine, adjusted for sex, height, time of day, outdoor temperature and

relative humidity at the time of the test, and housing tenure. These results are based on 757 children with complete spirometric and salivary cotinine data. Forced vital capacity was unrelated to cotinine concentration, but all other indices decreased with increasing exposure. This trend was more apparent for end-expiratory flow rates, the trends for FEF75-85% and FEF75% being significant at the 5% level. The consistency of these effects may be contrasted with the weak and inconsistent effects of number of smokers in the household on the same spirometric indices (Tables 22 and 23).

Table 31 shows the relationship between exercise-induced bronchospasm and quintiles of salivary cotinine among 755 children who completed a satisfactory exercise test and on whom saliva assay results were available. Across the whole table, there was no trend towards more bronchospasm in the children with high cotinine levels (X^2 for trend 0.08, 1 df). Similar results were obtained for each sex, and for children with and without a history of wheeze.

A decline in FEV1 of more than 10% after exercise was most common in the fourth quintile of salivary cotinine (1.3-3.5 ng/ml), reflecting the high prevalence of wheeze in this group (Table 29). However, the

prevalence of reactivity in the uppermost quintile was unremarkable.

4.5.3. Impedance Tympanometry and Salivary Cotinine

Satisfactory tympanograms were available for 736 (96%) of the 770 children with salivary cotinine data. When cotinine levels were grouped into quintiles, there was a highly significant trend (X^2 for trend 7.01, 1 df) towards more abnormal tympanograms in the children with higher levels of cotinine (Table 31). In view of the association of cotinine with sex and housing tenure (Table 28) and the modest effect of these factors upon the prevalence of effusion (Table 25), the relationship between salivary cotinine and middle ear effusion was analyzed further by multiple logistic regression. Presence or absence of effusion (Type B tympanogram) was treated as the outcome variable, and the cotinine data were fitted as a continuous explanatory variable. A logarithmic transformation of the cotinine concentration was again found to give the best fit, its relationship to the risk of Type B tympanogram (middle ear effusion) being very close to linear on a logit scale (X^2 for inclusion of quadratic term 0.0002, 1df).

In single-factor models, the odds ratio for female sex was 1.53 (95% confidence interval 0.93-1.98) and for rented housing was 1.43 (0.84-2.42). The effect of log

cotinine in a single-factor model was significant (X^2 6.60, 1df), and the odds ratio per doubling of cotinine concentration was 1.14 (1.03-1.27). In a joint model including all three factors, the effects of sex and log cotinine changed little, but there was an appreciable reduction in the odds ratio for rented housing, suggesting that passive smoke exposure explained much of the effect of housing tenure in the single factor model. The adjusted odds ratios were 1.46 (0.87-2.44) for female sex, 1.03 (0.55-1.91) for rented housing, and 1.13 (1.00-1.28) per doubling of salivary cotinine concentration. The effect of log cotinine remained significant in the joint model (X^2 4.14, 1 df).

The linear relationship between log cotinine and the prevalence of disease on a logit scale implied that the prevalence odds was proportional to a power of the cotinine level, the power exponent being the coefficient (log odds ratio) for log cotinine in the logistic model. The data suggested that the odds ratios for Type B tympanograms after adjustment for sex and housing tenure, relative to children with undetectable levels of cotinine, would be approximately 1.7 at 1 ng/ml and 2.3 at 5 ng/ml. Thus, even low levels of passive smoke exposure may have substantial effects upon the prevalence of middle ear effusion.

The model would predict that in a population of children with the same sex and tenure distribution, all of whom had undetectable levels of cotinine, the prevalence of Type B tympanograms would be approximately 5.8%. As the observed prevalence was 9.4%, at least one-third of middle ear effusions in the study sample were statistically attributable to passive smoking.

5. DISCUSSION

5.1. Measurement of Ventilatory Function in Seven-Year-Old Children

Seven-year-old children were chosen for this study because they were considered to be old enough to cooperate with lung function testing, but young enough for effects of active smoking to be essentially excluded. Furthermore, several large epidemiological studies of asthma among children of this age (110-112) have demonstrated a high prevalence of potentially treatable morbidity, which tends to disappear as the children grow older (110,111). Although pre-school children may be more constantly exposed to adverse factors in the home, the scope of ventilatory function testing is severely limited before five years of age (190). Indeed, it was apparent during the fieldwork that the school year chosen was the youngest from whom reasonably reliable spirometric results could be expected. Several of the smallest children (some of whom had yet to reach their seventh birthday) experienced difficulty in prolonging their forced expiration beyond one second. The choice of a study population which was marginal in terms of ability to cooperate with ventilatory function tests implied that particular attention should be paid to the

repeatability of spirometric indices and to the definition of abnormal bronchial lability.

5.1.1. Repeatability of Spirometric Indices

Few publications present data relating to within-subject variability of ventilatory function in children. In their extensive review, Polgar and Promadhat (190) quote only one early study using reverse plethysmography (191). Within-occasion variability of vital capacity and FEV1/VC ratio were assessed in 55 children aged 6-14 years, 38 of whom had asthma. The within-subject standard deviation of VC (78 ml) was comparable to that obtained for FVC in this study (81 ml) (Table 1). In more recent publications, the emphasis has been upon between-occasion variability in older children. Leeder et al. (192) measured FVC, FEV1, FEV0.5, PEFR and flow rates at 50% and 75% of forced expired vital capacity by pneumotachograph weekly over a six week period in 19 girls of mean age 15.8 years. They quote standard deviations for readings in the same subject on different occasions of 166 ml for FVC and 155 ml for FEV1, and comment that the ratio of within-subject variation to between-subject variation was greater for flow rates than for lung volumes. Hutchison et al. (193) performed repeated lung function tests on 20 healthy children (11 male) aged 10

to 16 years, using spirometry to determine lung volumes and body plethysmography to determine flow rates. No significant effect could be determined from time of day, nor from the retest interval up to two months. Pooled within-subject standard deviations can be derived from their data; 90 ml for FVC and 112 ml for FEV1. Again, variability in flow rates was significantly greater than for lung volumes.

In view of the much younger children studied here, it is surprising how closely the within-subject variability of FEV1 and FVC, both within occasions and between occasions, compare with the published reports. When considered in absolute terms, it appears that the between-occasion standard deviation for FEV1 and FVC may be substantially independent of age, and of the order of 100-150 ml for each index. This would be consistent with the observations that in older children, the standard deviation of FEV1 was independent of the actual volume expired in one second (193), and implies a smaller coefficient of variation with increasing lung volume. Among the seven-year-olds in the present study, there was a weak inverse relationship between within-subject, between-occasion standard deviation and mean level of FEV1. This may reflect the fact that the smaller, younger children were close to the age limit at which reproducible

spirometry is feasible. Alternatively, children with reactive airways may have had spontaneous bronchospasm at one attendance which both lowered their mean achieved FEV1 and increased the variation between the two recordings.

5.1.2. Measurement Error and Biological Variation

For epidemiological studies which concentrate upon baseline spirometry, between-occasion variability is of greatest importance. The subdivision into within-occasion ("measurement error") and true between-occasion ("biological") variation (Table 3) suggests that for most indices, and particularly for FEV1, biological variation is of considerable importance. This limits the opportunity for improving precision simply by repeating spirometry at the same test session. Substantial reduction in variability may require repeated recordings in the same subject over a period of days or weeks. The resulting gain in precision may be essential where the objective is to measure growth or changes in ventilatory function over a prolonged period (192). However, where baseline spirometry itself is to be compared between individuals in a population, financial and logistic considerations may suggest that it is more efficient to increase the

sample size, rather than to attempt repeated measurements on a limited number of children.

The epidemiological approach to aetiological investigation relies upon naturally occurring variation in disease characteristics. Where these characteristics are measured imprecisely, spurious variation arises between subjects in a population, which is of no aetiological relevance. Statements about the proportion of variance explained or unexplained by putative causes may be misleading if they do not take this into account. Table 4 emphasizes that within-subject (between-occasion) variability, height and sex account for about half of the between-subject variation in most spirometric indices at seven years of age. The corollary of this is that the amount of "unexplained" variation is substantially smaller than estimated from typical epidemiological data, but the proportionate contribution of factors which do explain some of the true between-subject variation is correspondingly greater.

5.1.3. Definition of Abnormal Bronchial Lability

The estimates of within-occasion variability were of particular interest in this study, where one of the principal outcomes was a short-term change in ventilatory function. In evaluating any diagnostic or

screening test, high repeatability is a necessary, but not sufficient, condition for high validity. Thus, forced vital capacity may be one of the more repeatable lung function indices, but it lacks validity as a measure of airway calibre. Both PEFR and FEV1 have been widely used to measure bronchospasm in physiological and pharmacological challenge tests. It has been suggested that in children given a graded histamine challenge, the proportionate changes in each index are approximately equal, and that PEFR can be used interchangeably with FEV1 (194). Table 2 demonstrates that, for any given criterion of abnormality, a test based upon changes in FEV1 will be considerably more specific than the equivalent test based upon PEFR. The choice of a 20% reduction in FEV1 as the conventional criterion of abnormality (195) appears to be justified, even in this young age group. On purely statistical grounds, there must be considerable reservations about the predictive value of lesser degrees of bronchospasm, particularly when these are measured using PEFR (159,160). Repeatability is of particular relevance when multiple comparisons are made. The greater precision of measurement for FEV1 may be essential if ventilatory function is to be measured after graded doses of a pharmacological challenge (Table 2).

With these considerations in mind, FEV1 was chosen as an intrinsically valid and reasonably repeatable measure of post-exercise bronchospasm. Measurement error (within-subject variability) will, nevertheless, have resulted in misclassification of individuals according to their degree of bronchial lability, and as a result, relationships between lability and symptoms, or between lability and environmental exposures will be attenuated. Applying the estimates of variability presented in Table 1, among one hundred children with a 10% reduction in measured FEV1, 12 would have a true reduction of 15% or more, and 13 a reduction of 5% or less. Such calculations, and those in Table 2, make the improbable assumption that the true within-subject variability is identical for each subject. In fact, it is likely that some children perform much more consistently than others, so the estimates of false positive rates for different test criteria may be too conservative. The resolution of this uncertainty would be complex, requiring repeated tests on each child to determine within-subject variability for each individual.

5.2. The Nature of Childhood Asthma

5.2.1. Symptoms and Bronchial Lability

The distribution of exercise-induced bronchial lability (Figure 1) suggested a continuum of airways reactivity, with no evidence of bimodality. This may be due to random error in the measurement, which could blur a distinction between an "abnormal" group and the remainder of the population, but it supports the concept of asthma as a single disease, with a spectrum of severity (111,112). On the other hand, only one-sixth of the children reported to have wheezed in the past year demonstrated unequivocal exercise-induced bronchospasm, and another 10% might have done so if their treatment had been withdrawn (Table 7). In nearly two-thirds of the children with recent wheeze, exercise affected their FEV1 by less than 10%, and it must be questioned whether these children had clinically relevant exercise-induced asthma at the time of the test.

There has been some debate as to whether challenge tests detect abnormal airways reactivity among currently asymptomatic individuals ("latent asthma") (196), or whether the underlying hyperreactivity follows the time course of symptomatic asthma (158). The absence of any association between past wheeze and

bronchial lability (Table 7) tends to favour the latter suggestion. Similarly, there was little evidence that a prior history of bronchitis or pneumonia resulted in abnormal lability, in the absence of recent wheeze. On the other hand, children with a history of lower respiratory disease in the past had evidence of abnormal baseline spirometry, particularly when expressed as a ratio of forced vital capacity (Tables 5 and 6). This was not attributable to respiratory symptoms in the week prior to the test, nor to recent wheeze which, as expected, was strongly related to impaired baseline spirometry (197). The absence of any association between past lower respiratory disease and exercise-induced bronchial lability suggests that the abnormalities of baseline ventilatory function in this group do not reflect temporary bronchospasm, but are a manifestation of longer-term impairment. This important distinction has not hitherto been addressed by population-based studies (198,199), although it has been recognized in prospective studies of children admitted to hospital with lower respiratory illness in infancy (200,201). One explanation for such reduction in ventilatory function would be that it reflects structural "lung damage" following chest illnesses in early childhood. Alternatively, there may be perinatal influences on lung development which render the young

child susceptible to lower respiratory illnesses and, independently, impair ventilatory function in later life. Suggestive evidence that ventilatory abnormalities in young infants may precede the development of chest illness has recently been reported (202).

Other symptoms which are associated with asthma, such as recurrent nocturnal cough or a tendency for colds to go to the chest, appeared to have a weak association with measured bronchial lability, once the presence of recent wheeze was taken into account (Table 8). This supports the growing consensus that, for epidemiological purposes, wheeze may be regarded as the cardinal symptom of asthma in children (119). Additional evidence in this regard is provided by the relatively normal baseline spirometry among children with chest colds in the absence of wheeze (Tables 5 and 6) and the different social class distributions for wheeze, chest colds and nocturnal cough, discussed further below.

The exclusion of recurrent nocturnal cough from an epidemiological case definition of childhood asthma should not necessarily deter the clinician from considering inhaled bronchodilator therapy when faced with a patient presenting with this symptom in the

absence of wheeze (127,128). In the present study, there were three children (0.3%) who had multiple respiratory symptoms with exercise-induced bronchospasm, in the absence of wheeze (Table 8). These children might have benefited from such a therapeutic trial of bronchodilator therapy. However, it must be questioned whether a screening programme based upon exercise testing in general practice (159) would be justified to identify such a low prevalence of undetected but potentially treatable morbidity.

5.2.2. Relationship to Parental Social Class

Scadding (150) has pointed out that no one challenge test can adequately define asthma, which should be regarded as a manifestation of abnormal airways reactivity which may result from a variety of environmental stimuli. This limitation clearly applies to the exercise challenge used in this study. However, even if it characterizes only a subgroup of wheezy children at any one time, the relationships of exercise-induced bronchospasm to social and environmental variables can assist in the interpretation of symptoms reported by questionnaire. This application was demonstrated when lability and symptoms related to asthma were analyzed by parental social class (Table 9). The distributions of both

wheeze and bronchial lability were consistent, being relatively independent of social status, but there was an excess of nocturnal cough and chesty colds among the poorer families. The contrast between these distributions suggests that the preponderance of the less specific asthmatic symptoms in the lower social classes was due to factors unrelated to abnormal airways reactivity.

The overall prevalence of wheeze in the past year in this Edinburgh population was 12.5%, which is consistent with earlier studies of this age group (111-113). Rigorous comparisons cannot be made due to variations in the case definition and methods of ascertainment used in each survey. In common with these other studies, only about half of the wheezy children had ever been diagnosed as asthmatic. Current diagnostic practice in Edinburgh appeared to reflect the even distribution of wheeze across social classes (Table 9), although the somewhat lower prevalence of diagnosed asthma and inhaler treatment in class IV/V was reminiscent of recent social class differentials in disease labelling (113-116). Here, as in Tyneside (121), the use of asthma as a diagnostic label appeared to be a prerequisite for prescription of inhaled bronchodilator therapy. This raises concerns about the adequacy of treatment for the children whose wheeze was

not diagnosed as asthma, who comprised nearly half of all those with a history of this symptom in the past year.

The even social class distribution of wheeze, which is confirmed by the objective measurements in this study, contrasts with the marked differentials displayed by many common lower respiratory infections in early childhood. At the broadest level, this argues against an infective cause for the asthmatic trait, and suggests that the focus of aetiological enquiry should move away from the home and family circumstances towards, on the one hand, individual characteristics such as genetic constitution or obstetric history, or on the other hand, environmental factors affecting whole populations (119).

5.3. Housing Conditions and Respiratory Disease in Childhood

5.3.1. Overview

Respiratory conditions are those most widely associated with unsatisfactory housing conditions by the public (34,58). Young children are particularly suitable for studying potential adverse effects because they are exposed to the home environment for long periods in the

pre-school years, they may be more susceptible than adults, they are unlikely to smoke and are free from occupational hazards. Due to the need for objective spirometric data, this study included children who were already at school. Associations between respiratory disease and the home environment may therefore have been attenuated by the common exposure to the school classroom. The conclusions that can be drawn are necessarily limited by the cross-sectional nature of the study, which implies that measures of current exposure were used as surrogates for actual exposure over a prolonged period of time, or at some critical age in the past. Nevertheless, the findings relate to a wide range of housing characteristics and may usefully point to the relative importance of various aspects of the home environment for different measures of morbidity.

Overall, "lower" respiratory symptoms were more closely related to the housing characteristics studied than were "upper" respiratory symptoms. Cough, both during the day and at night, was associated with rented housing, parental smoking and increased housing density. Although cough was more common in damp and mouldy homes, this was largely due to confounding by these other factors. The effect of passive smoking, as indicated by salivary cotinine levels, was in the

expected direction, but after adjustment for housing tenure, neither day cough nor night cough were strongly or significantly related to salivary cotinine (Table 29). This contrasts with the dose-response relationship for cough found in several larger studies which ascertained parental smoking habits by questionnaire (89).

Wheeze showed a different pattern, with a strong relationship to dampness and mould growth, which explained the excess of wheeze in rented housing. The absence of any relationship between parental smoking and wheeze is inconsistent with some previous studies (89,95,203,204). Indeed, a recent national survey suggested that wheeze was the respiratory symptom most closely associated with parental smoking, particularly in Scotland (89). However, other studies have reported no relationship between parental smoking and wheeze or diagnosed asthma (113,205,206). One study using a cold air challenge found no significant association between bronchial reactivity and parental smoking (207) despite a relationship with wheeze (204). In the present study, salivary cotinine was not related to either wheeze or exercise-induced bronchospasm, so the role of passive smoking as a determinant of asthma requires clarification. It has been suggested that the effect of parental smoking upon bronchial reactivity may be

greater in males (208) or restricted to asthmatic subjects (209), but there was no evidence of such interactions in our data.

A tendency for colds to go to the chest shared some of the characteristics of cough, and some of wheeze. Earlier, it has been argued that, among non-wheezers, this symptom is unlikely to reflect underlying airways reactivity. Its epidemiological characteristics may depend upon two subgroups of "chesty" children; those with asthma (who are chesty as a result) and those without (whose chestiness is related to factors promoting respiratory infection or airways irritation). The latter group may account for the significant association with passive smoking, as indicated by salivary cotinine concentration (Table 29).

Apart from housing tenure, crowding, parental smoking, dampness and mould growth, the home environment was not found to be an important determinant of respiratory symptoms. Although the proportion of homes using bottled gas or paraffin heaters was rather low, the absence of any substantial effect from gas cooking suggests that hazards due to ambient nitrogen dioxide are small and difficult to detect in this age group. However, even a small risk associated with such a widespread and potentially remediable exposure might be

of considerable public health importance. As a recent review has emphasized, such low-level risks can only be adequately assessed by studies running into tens of thousands of children (7).

Baseline spirometry was closely related to recent wheeze and to a past history of lower respiratory infection. It might be expected that, as continuous outcomes, spirometric indices would be sensitive markers of adverse effects from the home environment. On the other hand, effects on lung growth might take years to develop. Studies of the effects of parental smoking and gas cooking on lung function in primary school children have generated conflicting results (4,6). In this study, cooking fuel was one of the housing factors with greatest influence, but the only significant effects were for mid-expiratory flow rates. It may be of relevance that these were also the spirometric indices most sensitive to medical history.

Parental smoking, as reported in the questionnaire, was not found to be related to ventilatory function, but most baseline spirometric indices decreased with increasing levels of salivary cotinine (Table 30). End-expiratory flow rates showed the strongest association, which was significant after adjustment for sex, height and housing tenure. Although the difference in FEF75-

85% and FEF75% between top and bottom quintiles of salivary cotinine was modest in terms of immediate clinical significance, it might be interpreted as evidence of damage to the smaller airways which could later progress to more severe impairment, as has been observed in some (94,210), but not all (211), longitudinal studies, and in a retrospective study of young adults (97).

Two associations that emerged strongly from the data were those between parental smoking and tympanometric abnormalities, and between damp, mouldy housing and wheeze. These are discussed in greater detail in the following sections.

5.3.2. Passive Smoking and Middle Ear Effusion

This is the first study to report biochemical data relating to passive smoke exposure in primary school children. The age group chosen were young enough to exclude regular active smoking, but some of the higher levels of salivary cotinine observed were greater than could reasonably have been attributed to passive exposure. These high levels may indicate experimentation with cigarettes, even at this early age. However, none of the six children with cotinine levels above 15 ng/ml had middle ear effusion (five had normal Type A tympanograms), so that their inclusion in

the analysis will have tended to diminish any effects attributed to passive smoke exposure, rather than generate a spurious effect.

As expected, cotinine levels were related to the number of smokers in the home, but equally striking was the variation within groups with equal numbers of smokers, by sex and housing tenure (Table 28). Even among the children from non-smoking households, cotinine levels were higher in rented accommodation. This may reflect significant exposure outside the home, which is strongly related to social factors. After controlling for tenure and number of smokers, girls had higher salivary cotinine levels than boys. This may reflect sex differences in cotinine metabolism or in activity patterns, boys being perhaps more likely to play outdoors or away from actively smoking adults.

The prevalence of tympanometric abnormalities in this seven-year-old population is consistent with published reports (180,181). Longitudinal studies in this age group have demonstrated that many of the abnormalities detected in a prevalence survey, including cases of effusion, tend to resolve spontaneously (182). The spectrum of disease in this population therefore probably represents a dynamic situation in which middle ear disease is in some children progressing towards,

and in others regressing from, severe underpressure and effusion. On the other hand, validation of tympanometry in children attending for myringotomy (176-178) has suggested that the dichotomy between peaked (A and C) and flat (B) tympanograms has greatest predictive value in the diagnosis of middle ear fluid. The analysis therefore treated middle ear disease both as a spectrum and as a dichotomy between peaked and Type B tympanograms. It is reassuring that similar results were obtained from both methods.

The middle ear effusions as defined here probably included only a few persistent cases in whom surgical intervention would be indicated. The findings are therefore complimentary to, rather than directly comparable with, case-control studies of children admitted to hospital (99-101). They do, however, relate to an age-group close to the peak age for admission for surgery for glue ear (166). The advantage of population-based measurements is that they avoid the potential selection biases of studies based upon hospitalized patients, which may derive from the powerful influence of the "health culture" of the family (102) and variations in local clinical practice (168).

The results demonstrate a significant relationship between salivary cotinine levels and middle ear pathology, whether considered as a spectrum of tympanometric abnormality, or as a dichotomy between tympanograms with and without a definable peak, taken to indicate effusion. It is unlikely that these associations were due to bias, since the disease is largely asymptomatic, the measurements were fully objective and the laboratory analysts were blind to the tympanometric findings. Adjustment of the crude estimates of the cotinine effect for sex and housing tenure indicated some confounding by these factors, but it is unlikely that residual confounding by socio-environmental factors persisted in the final model. The coefficient (log odds ratio) for housing tenure after adjustment for sex and salivary cotinine concentration was close to zero, and further adjustment for a range of more specific housing characteristics made little difference to the results (Section 4.5.3.).

On the other hand, the salivary cotinine levels relate only to passive smoke exposure in the previous two or three days; variation in exposure from week to week limits the reliability of a single measurement. The true association between passive smoking and middle ear effusion is therefore underestimated in this data (188). It might also be argued that controlling

imprecisely for cotinine level substantially reduced the effect of tenure upon risk of middle ear effusion in the joint model, so that if a more precise estimate of exposure had been available, this residual confounding by housing conditions might disappear altogether. This would be consistent with the lack of relationship between tympanometric findings and parental social class (Table 25).

The relationship between passive smoke exposure and middle ear effusion is consistent with three case-control studies (99-101) and one population survey (103). Four other population surveys (104-107) found no relationship, but this may reflect the younger age groups studied, there being a suggestion that the risk associated with parental smoking increases with age (103). The common mechanism in the pathogenesis of serous otitis media is considered to be loss of patency of the Eustachian tube, to which anatomical factors, mucociliary function and upper respiratory infection or allergy may contribute (164). Passive smoking might increase the risk of Eustachian tube blockage in a number of ways; direct impairment of mucociliary function, congestion of the soft tissues of the nasopharynx or predisposition to upper respiratory infection. With data derived from a prevalence study, it is unclear whether smoke exposure influences the

incidence or the persistence of the effusion, but both are of relevance in determining the impact of the disease.

Concern has been expressed recently that the documented risks of passive smoking have not included reference to middle ear effusion (212). In view of the important health service burden posed by glue ear and lingering suspicions of its long-term effects upon linguistic and cognitive development, middle ear effusion should be regarded as one of the more significant hazards attributable to environmental tobacco smoke.

5.3.3. Damp, Mould and Wheeze; Validation of Symptom Reporting

A preliminary study had suggested an inconsistency in the relationships of damp housing to reported symptoms and to general practitioner consultations for respiratory illness (1). This raised concern that the association between mould and wheeze in questionnaire data might be due, at least in part, to differential reporting behaviour. In a study of adult respondents, 43% of those living in areas of poor quality housing associated respiratory symptoms with their housing situation, whereas in areas of good housing only 10% did so (58). Differences such as this may reflect a causal relationship, but they raise the possibility

that reports of health status, particularly respiratory symptoms, may be influenced by perceptions of the home environment. The present study demonstrated that, at any given level of exercise-induced airways reactivity, the prevalence of wheeze reported by parents of children from homes with mould was substantially higher than the prevalence reported among children from unaffected homes (Table 17).

Interpretation of these results depends upon the validity of the exercise challenge as an objective indicator of the disease of interest. Lack of sensitivity and random errors in the test procedure may have reduced the power of the study to detect a true relationship between reported mould growth and bronchial lability, but these limitations cannot explain the different relationships between wheeze and lability among the children from homes with and without mould.

This difference could be explained if exposure to mould commonly resulted in a syndrome (or a subtype of asthma) which caused wheeze but which was not associated with airways reactivity to exercise. By its very nature, this would be a difficult proposition to test objectively, but it is considered unlikely for two reasons. Firstly, epidemiological (111,112) and

clinical (121) evidence supports the concept of childhood asthma as a single disease, the cardinal symptom of which is wheeze. Secondly, the most plausible causal mechanism for any association between mould and wheeze would be allergy to airborne spores, but atopic skin reactions to common antigens are associated with more frequent wheeze (120,153), and atopic children are more likely to have demonstrable airways reactivity (112,152).

An alternative argument might be that exercise-induced bronchospasm reflects underlying susceptibility to asthmatic attacks, rather than the activity of the disease itself. Then, the prevalence of symptoms might depend upon both host factors (non-specific bronchial hyperreactivity) and the "dose" of trigger factors in the environment (including mould spores). The results presented in Table 17 could be interpreted in this way, given that exercise-induced lability was an imprecise measure of underlying airways reactivity, and that mould may not be a trigger for all susceptible children. However, such a distinction between host and environmental factors is called into question by observations that when patients with house dust mite sensitivity move to an allergen-free environment, there is a reduction in the response of their bronchi to pharmacological challenge (43,148). This suggests that

non-specific bronchial hyperreactivity can result from allergen exposure, and should rightly be considered a manifestation of asthma, rather than a cofactor in its aetiology. The observation, in this study, that past wheeze was unrelated to current bronchial lability (Table 7) is more consistent with this latter view.

The most straightforward explanation is that awareness of dampness or mould in the home influences the way in which parents report respiratory symptoms, and that much of the association of damp, mouldy housing with respiratory symptoms can be accounted for by reporting bias. The use of the term reporting bias should not be misunderstood. It does not mean that the accuracy of reporting is necessarily poorer in mouldy homes; it is possible that recall is actually less complete for children in homes unaffected by mould. However, its presence does imply that further studies of the same relationship which rely on questionnaire information alone are unlikely to be valid.

5.3.4. Objective Measurements of the Home Environment

If dampness in the home is identified as a cause of ill-health by the general public, a second type of reporting bias could arise. Parents of symptomatic children may become more aware of adverse home conditions whilst attempting to explain the occurrence

of symptoms in their child. The possibility of this type of information bias has been addressed by two previous studies (33,34), and one which was published after completion of the present survey (31).

Two studies (31,34) validated reports of dampness using independent assessments by environmental health officers. One found a high degree of concordance (34), but in the other (31), parents and EHOs disagreed about the state of damp and mould in 31% of the dwellings. The use of EHO assessments is attractive in that it considers dampness in its entirety, using criteria which decide priority for rehousing. However, such a global assessment may be less useful where the aim is to set quantitative building standards (5). Also, it is unclear to what extent independent observers might be influenced by comments or guidance from the householders, particularly in the location of patches of dampness or mould growth behind furniture or household appliances.

Melia et al. (33) used thermohygrographs similar to those in the present study, although they did not control for climatic variation. The humidity levels reported were higher than we recorded in Edinburgh homes, but this may be due to exceptionally low levels of outdoor vapour pressure during the winter months of

our study. They found a significant excess of lower respiratory symptoms in the children with the most humid bedrooms, but these data relate to only 44% of their target sample. It is possible that families who were aware of both dampness and respiratory problems were more likely to have responded to their survey, and because the information about symptoms was collected after the thermohygrograph recordings, no assessment of such bias was possible.

In the present study, an encouraging response was achieved from a sample of the general population, and non-response bias appeared to be minimal. No relationship was found between environmental measurements and any of the objective measures of respiratory abnormality: baseline spirometry, exercise-induced bronchospasm or middle ear underpressure and effusion. Furthermore, the absence of any clear association with symptoms (Tables 19 and 20) suggests that the associations between chest complaints and damp housing which were observed in the questionnaire data (Tables 15 and 16) may be, at least in part, due to differential reporting of dampness in the home, depending upon the presence or absence of symptoms in the child.

The interpretation of these negative findings rests upon the validity of the objective indices chosen to measure "dampness" and the power of the study to detect true effects of a magnitude which would be considered of public health importance. Related to both these issues is the effect of random errors in the measurements which tend to attenuate real associations and reduce the power of significance tests. An additional consideration may be reverse causality; that is, the effect of chronic respiratory disease in the child upon parental decisions about heating and ventilation in the child's bedroom. In this regard, it is relevant to note that no excess of symptoms was observed in the warmest, driest bedrooms (Table 20).

Wheeze was one of the less prevalent symptoms, but it was the complaint which might be expected to show the closest association with humidity. With a true overall prevalence of 12% for wheeze in the past year, a difference between a prevalence of 6% in the lowest tertile of temperature or relative humidity and 18% in the top tertile might be of considerable research and policy interest. The study of 317 homes had a power of 77% to detect such a trend as significant at the 5% level, and correspondingly greater power for more prevalent symptoms. Furthermore, many of the observed differences in temperature and relative humidity

between symptomatic and asymptomatic groups were close to zero, implying that a very much larger study would have been required to demonstrate them as statistically significant. The public health importance of such minimal effects must be questioned.

Ambient relative humidity was readily monitored in an objective and standardized manner, but limited equipment and manpower inevitably resulted in recordings spread over a number of weeks. This is the first study to attempt an adjustment for climatic variation, but, strictly, our procedure may not be generalizable beyond the five homes from which it was derived. The additional analyses using a simultaneous semi-quantitative estimate of relative humidity go some way towards meeting such reservations (Table 19).

A more serious criticism of these findings is that airborne humidity may be a poor indicator of biologically relevant exposure. House dust mites thrive in homes considered to be damp, and may be difficult if not impossible to eradicate from such environments (39). However, it is reasonable to suppose that this is because the relative humidity in soft furnishings is influenced by the ambient humidity of the room (37), an environmental exposure which was directly measured in this study. On the other hand, reported dampness, which

was associated with respiratory symptoms, was not a good predictor of humidity ranking. This is probably because the formation of patches of condensation on walls depends upon the temperature of the wall (reflecting the efficiency of insulation) as well as the humidity of the air in the room. The relative humidity of the cold or moist indoor microenvironments suitable for mould growth (16) may be poorly represented by measurements of the air in one room of the house.

In a case-control study of adult asthma, visible mould in the home was more reported more commonly by cases (49), and in the questionnaire survey reported here, associations with reported mould were generally stronger than with dampness. Obtaining precise and objective information about levels of exposure to specific indoor moulds is a highly complex and labour intensive procedure (21), but Platt et al. (31) report associations of respiratory morbidity in children with total (all-species) counts of viable mould spores obtained from air samples in their homes. Total mould spore counts were only weakly correlated with the degree of dampness and mould growth reported by parents ($r = 0.14$). Associations of reported respiratory symptoms in children with parental assessments of the home environment were stronger than with mould spore

counts. This may reflect the high degree of variability of mould spore counts over time (21), but would also be consistent with reporting bias. This author has suggested that the issue of parental reporting behaviour could be addressed further by separate analysis of the 31% of children for whom subjective and objective assessments of the home environment differed (214).

6. CONCLUSIONS

6.1. Summary of Main Results and Conclusions

1 One in eight children in Edinburgh had a history of wheeze in the past year at age seven. Almost half of these had used a bronchodilator inhaler over the same period. Use of the diagnostic term asthma appeared to be a prerequisite for provision of inhaled therapy. This raises concerns about the adequacy of diagnosis and treatment among the other half of the wheezy children.

2 Estimates of the within-subject repeatability of spirometric indices in this seven-year-old population suggest that FEV1 is the most reliable index of airway calibre, and that a 20% change in FEV1 would occur by chance alone less than once in one thousand bronchial challenge tests. The value of peak expiratory flow measurements appeared to be severely limited by their greater within-subject variation.

3 Wheeze in the past year was strongly related to reduction in FEV1 after a six minute free running exercise challenge, but in two-thirds of the children with recent wheeze, exercise affected FEV1 by less than 10%. The distribution of exercise-induced lability among children with wheeze in the past, but none in the previous

twelve months, was similar to that in the remainder of the population. This suggests that non-specific airways reactivity is a manifestation of active disease, and not an indicator of constitutional susceptibility to asthma.

4 Nocturnal cough, chesty colds and a history of bronchitis or pneumonia were more common among wheezy children. Among non-wheezy children, however, they were unrelated to exercise-induced bronchospasm, suggesting that airways reactivity is not a major cause or consequence of non-wheezing chest illnesses.

5 After adjustment for sex, height, time of day, and outdoor climatic conditions, baseline spirometric indices were, as expected, consistently lower in the children with wheeze in the past year. This effect was most marked for mid-expiratory flow rates, which may deserve greater attention in clinical and epidemiological surveys. Among those without recent wheeze, a tendency for colds to go to the chest was weakly associated with impaired ventilatory function. A history of wheeze, bronchitis or pneumonia in the past was more strongly and consistently related to poor baseline spirometry. These effects were independent of recent wheeze, chesty colds or upper respiratory

symptoms prior to the test, so it is unlikely that they were the result of continuing airways reactivity. The findings therefore offer support for an association between permanent lung damage and lower respiratory illnesses in early childhood.

6 Wheeze and exercise-induced bronchial lability were not related to parental social class. This was in contrast to marked social class trends in recurrent nocturnal cough and chesty colds. Asthma was less likely to be diagnosed among wheezy children from the families of manual workers, but this difference was small. This suggests that social class differentials in diagnosed asthma in the recent past were artifacts of labelling and implies that current diagnostic practice reflects more accurately the nature of the underlying disease. The even distribution of wheeze and bronchial lability across social classes argues against an infective aetiology for the asthmatic trait. It may indicate that the important determinants of childhood asthma are to be found among environmental factors affecting whole populations.

7 Middle ear effusion was detected by impedance tympanometry in 10% of the children, 3% having

bilateral effusions. Effusion was closely related to recent pain or discharge in the ear, but was not associated with wheeze or hay fever. It would appear that infection is more important than atopy as a cause of middle ear disease in this age-group. The prevalence of effusion was three times greater among children with a history of tonsillectomy or adenoidectomy, suggesting that surgical relief of proximal Eustachian tube blockage may not have the expected long-term protective effect in children susceptible to secretory otitis media.

8 Fourteen features of the home environment were defined from questionnaire data: tenure, persons per room, number of smokers, gas cooking, coal fire, bottled gas, paraffin heater, wood stove, damp patches on walls, patches of mould or fungus, and the following characteristics of the child's bedroom during the winter months: number sleeping there, heat at night, heat during the day, and window open at night. Dampness was reported in 8% of owner-occupied homes and 30% of rented homes. The corresponding figures for mould growth were 5% and 19%. Measurements of temperature and relative humidity were obtained by seven-day monitoring in one-third of the homes. There was a poor

correlation between reported dampness and measured relative humidity, and the distinction between the two may be biologically relevant. Ambient humidity is probably the more important determinant of house dust mite populations, whereas mould growth is more closely linked to patches of condensation on walls and window sills.

9 Wheeze in the past year was unrelated to most features of the home environment, including parental smoking. There were, however, strong associations between wheeze, dampness and mould growth. The prevalence of wheeze in non-mouldy homes was 11%, compared to 38% among the children sleeping in mouldy bedrooms, and 23% among those in homes affected by mould elsewhere. These figures confirm the findings of the preliminary study in northwest Edinburgh and suggest that, statistically, mould in the home accounted for 14% of all cases of wheeze (6% of the cases in owner-occupied homes and 26% of the cases from rented housing). Among non-mouldy homes, housing tenure was not related to recent wheeze.

10 Dampness and mould growth were also strongly associated with chesty colds, night cough, day cough, but these were substantially explained by the primary association with wheeze and by the

confounding effects of housing tenure, crowding and parental smoking. Cooking and heating fuels did not appear to be important determinants of lower respiratory symptoms. Hay fever, ear trouble and sore throat showed no association with any housing feature. Nasal discharge resembled cough in its associations with rented housing and parental smoking.

11 In contrast to reported wheeze, exercise-induced bronchial lability differed little between mouldy and non-mouldy homes. However, at every level of measured exercise-induced bronchospasm, the prevalence of wheeze was substantially greater among children from mouldy homes. Various interpretations may be placed on this discrepancy, the most plausible being that parents who are aware of mould in the home report their child's symptoms differently from those that deny mould. This type of reporting bias casts doubt on the validity of previous surveys which have relied on questionnaire information to determine the relationship of respiratory symptoms to dampness or mould growth in the home.

12 Housing conditions in general, and parental smoking and gas cooking in particular, were not found to be important determinants of baseline

spirometry. Weak relationships were found between reported dampness and poor ventilatory function, with statistically significant effects on mid-expiratory flow rates, independent of tenure, crowding, gas cooking and parental smoking. Given that a history of wheeze in the past year was a major determinant of most spirometric indices, these findings emphasize the discrepancy between objective and subjective morbidity data.

13 Measurements of salivary cotinine, a biochemical marker of tobacco smoke exposure, provided a more sensitive test of adverse effects due to passive smoking. Cotinine was detected in the saliva of 85% of the children, and six children had levels suggestive of experimentation with active smoking. After adjustment for the number of smokers in the household, cotinine concentrations were higher among girls and children from rented housing. Although the associations of baseline spirometric indices with cotinine were stronger than with number of smokers in the household, only end-expiratory flow rates showed a significant reduction, after adjustment for sex, height and housing tenure. Wheeze and bronchial lability were not related to salivary cotinine.

14 Despite the lack of association between reported ear trouble and housing conditions, tympanometric evidence of middle ear effusion was more common in children exposed to tobacco smoke. Among those from homes where two adults smoked, the prevalence of effusion was 1.8 times that in non-smoking households. This latter effect was of borderline significance after adjustment for housing tenure and dampness. There was a non-significant excess of effusions among children from damp houses, but this was partly explained by the confounding effect of parental smoking. Tympanometric abnormalities and middle ear effusion were significantly related to salivary cotinine level, such that about one-third of all effusions in this age-group may be attributable to passive exposure to tobacco smoke.

15 Objective measurements of weekly mean temperature and relative humidity in the child's bedroom were unrelated to respiratory symptoms, exercise-induced bronchial lability, baseline spirometry, and middle ear effusion. Continuous monitoring of five homes over the four-month observation period confirmed that temperature and humidity ranking remained reasonably constant. It therefore appears unlikely that indoor temperature and humidity are

important determinants of respiratory morbidity in this age-group. The role of surface condensation and consequent mould growth is not directly assessed by these data. Further studies are required to address this issue.

6.2. Implications for Further Research

6.2.1. Damp Housing and Childhood Asthma

This study confirmed the finding of previous surveys in one part of Edinburgh (1,34), suggesting that an association between damp or mouldy housing and respiratory symptoms is not confined to specific council estates, nor to rented as opposed to owner-occupied housing. The association between mould and wheeze met many of the criteria for considering an epidemiological association to be causal (213). It was strong, relatively specific when compared with other symptoms, consistent with previous studies and free of substantial confounding by other factors studied. Biologically plausible causal mechanisms can be proposed and, assuming that duration of exposure was greatest when the child's bedroom was affected, there was a suggestion of a dose-response relationship (Table 15).

On the other hand, the attempt to validate reported symptoms and housing conditions by objective measurements cast serious doubts upon the reality of this association. Assessment of bronchial lability by exercise proved highly acceptable to the children, and, being a common physiological stimulus, carried intrinsic validity. Although the prevalence of unequivocal abnormality was rather low, the analysis of lability as a continuum permitted a more powerful test of environmental effects. The problem with the exercise challenge appeared to be substantial random error in the measurement of exercise-induced bronchospasm, and lack of sensitivity to many cases of wheeze. It is possible that a pharmacological challenge would provide a more sensitive test of airways reactivity which might correlate more strongly with housing conditions, but imprecision in measurement of outcome becomes an increasing problem as the number of post-challenge tests increases (Table 2).

These observations highlight a fundamental problem in asthma epidemiology; there is no "gold standard" against which new procedures can be validated. Indeed, wheeze is a reasonable candidate for such a standard (119), which creates an immediate dilemma when the objective of the study is to validate symptom reporting. This is of particular concern in the light

of the present findings, which suggest that reporting bias may account for much of the observed association between damp, mould and wheeze.

One way forward might be to seek confirmation of respiratory ill-health indirectly through a number of measures, such as general practice consultations, hospital admissions and school absences due to asthma. All of these are to some extent dependent upon parental behaviour, but they may be more direct measures of morbidity than clinical tests of abnormal airways physiology.

If disease status is to be assessed with reference to the medical care process, then measurements in the home could be obtained much more efficiently than was possible in the context of this cross-sectional study. Although care was taken to correct temperature and humidity measurements for climatic variations, by continuous monitoring of selected homes, the assumptions on which this was based could be challenged. A matched pair case-control design would allow a more precise adjustment for seasonal effects, if home monitoring proceeded simultaneously in the homes of each case-control pair, and the results were analyzed as matched sets. However, such a design presumes a dichotomous definition of disease, which may

poorly represent the spectrum of manifestations that are currently recognized as asthma. Furthermore, possible selection effects in the identification of cases may complicate the choice of an appropriate control group.

An alternative line of enquiry would be to consider in more detail possible mechanisms that might account for a causal link between damp housing and respiratory disease. The problem with such information is that it may confirm that a causal link can exist, without establishing the extent to which it actually operates in the real world. Thus, immediate (Type 1) hypersensitivity to mould spores provides a plausible explanation for an effect of mould in the home upon symptoms related to asthma. Undoubtedly, a few patients can be found with positive inhalation challenge tests to specific mould spores, but, on the other hand, mould allergies are relatively uncommon causes of abnormal skin test reactivity in hospital practice (47) and many patients with positive results have multiple allergies. Although asthmatics with particular mould species in their home may have evidence of species-specific allergy which suggests a cause-effect relationship (49), the contribution of such allergy to their symptoms may be difficult to determine. The concentration of fungal spores in indoor air rarely

exceeds levels found commonly outdoors, and the contribution of indoor sources to the total inhaled spore burden is probably small (21). However, it can be argued that initial sensitization might arise through chronic indoor exposure (5).

In conclusion, we are faced with a dilemma. While case-studies of individual patients may raise the possibility of a health hazard, the contribution of dampness or mould growth in the home to the development of respiratory disease can only be quantified by epidemiological studies using clearly defined and validated definitions of exposure and outcome. Many of the difficulties in interpreting the results presented here arise from uncertainties about these definitions. Paradoxically, the more objective the data, the less clearly do they relate to the everyday experience of parents and their children. In the absence of clearly valid objective tests for asthma, the emphasis of future research should be upon more accurate characterization of the home environment and the use of case-control designs, where the cases are selected using a range of definitions, and the controls are chosen to minimize selection bias in the data. The drawback of these recommendations is that they focus attention upon one (or a few) disease outcomes, when a wide range of health effects may be of interest. The

strength of the cross-sectional design in the present study lies in the ability to study many disease-exposure relationships simultaneously, and to handle both continuous and discrete disease definitions.

6.2.2. Passive Smoking and Respiratory Health in Childhood

This is the first study to relate quantitative biochemical measures of environmental tobacco smoke exposure to indices of respiratory morbidity in children. The potential value of doing so is illustrated by the distribution of salivary cotinine concentrations among children from households reported as containing no smokers. These would normally be considered the "unexposed" reference category, yet almost three-quarters of this group had detectable cotinine in their saliva and 10% were in the upper two-fifths of the distribution of measured tobacco smoke exposure. Presumably this reflects smoking by visitors to the family or passive exposure outside the home, since none of the concentrations in children from no-smoker households were high enough to be compatible with active smoking. However, six children from smoking households had levels higher than would normally be attributable to passive exposure, and these may

indicate experimentation with active smoking, even at this early age.

Although biochemical markers permit accurate characterization of recent tobacco smoke exposure, they may not adequately reflect exposure at some critical period in the past. For instance, children attending school will tend to have lower levels of exposure to smoking by adults in the home than they had during their pre-school years. This may explain why the evidence of respiratory effects from parental smoking is most consistent in the first few years of life (4,6,84-86). Even if current exposure is of greatest relevance, within-subject variability of both cotinine concentrations (83) and spirometric indices (Table 3) will attenuate relationships between the two and reduce the power to detect true detrimental effects. Associations with salivary cotinine are therefore likely to underestimate the true relationship between passive smoking and respiratory morbidity.

Several cross-sectional studies have sought evidence of pulmonary damage attributable to passive smoke exposure in childhood. Where a range of spirometric indices are reported, as in this study, mid-expiratory or end-expiratory flow rates tend to be affected to a greater extent than FEV1 (215-219), although in one study flow

rates in early expiration were most affected (206), and in another the results differed between the sexes (95).

Further research using quantitative measures of exposure and more extensive adjustment for potential confounding variables is required to test these relationships more rigorously. The present findings suggest that such studies should include tests of end-expiratory airflow or small airways function and some assessment of tobacco smoke exposure from non-household members, both inside and outside the home. Large samples will be required to determine whether exposure to parental smoking in the pre-school years has long-term effects upon respiratory symptoms and ventilatory function in children of school age, independent of current exposure. Ultimately, the clinical and epidemiological significance of the small spirometric changes observed in cross-sectional studies can be assessed only by performing ventilatory function measurements repeatedly over time among children in whom active smoking is excluded, preferably by biochemical measurements.

6.3. Implications for Public Health Medicine

This study has addressed several questions of relevance to public health policy and practice. The two main disease outcomes, asthma and middle ear effusion, are highly prevalent among primary school children and make heavy demands upon general practitioner and hospital services. Both are of concern to parents and teachers because of their potentially damaging effects upon the child's education. Little is known about the aetiology of either disease.

In addition, asthma and its possible link with damp housing impinges upon the work of the community physician in an unusual way. Assessment of requests for rehousing on medical grounds is one of relatively few areas where community physicians deal with individual cases, albeit in the context of resource allocation within the community. A review of such assessments identified the link between unsatisfactory housing and asthma as one which was particularly difficult to determine (220). Thus, community physicians, general practitioners and other health service professionals might look to this study for guidance concerning the effects of damp housing upon respiratory health.

Unfortunately, statistical statements comparing average risk among groups of children are of most direct

relevance in the public health arena, such as development of building standards and regulations. They cannot adequately describe idiosyncratic reactions to an environmental exposure in a small number of highly susceptible individuals. The data suggest that dampness has little effect upon respiratory health for the majority of children. However, when faced with a decision to recommend rehousing or home improvements on the grounds that a child's housing is a hazard to their health, the general practitioner, community physician or environmental health officer should consider the epidemiological evidence in context, alongside the clinical history of each individual case.

The message for public health and housing policy is clearer. The association of damp, mouldy housing and respiratory disease will remain of concern to householders, and certainly deserves more thorough investigation. However, the results from this study do not suggest that a major shift of resources towards eradication of condensation and mould growth would have an important effect upon children's health. There are almost certainly more important gains for the public health from other improvements in the housing stock, particularly those based upon the implementation of existing standards of accident prevention, space heating and sanitation.

The study of salivary cotinine levels has added middle ear effusion to the growing list of health hazards that may be attributable to parental smoking. This relationship is consistent with some, but not all previous studies, and therefore requires replication before it can be regarded as fully established. It is unlikely that educational programs aimed at the control of adult smoking will benefit greatly from additional evidence of this transient and often occult effect upon child health. However, it may not be unreasonable to suggest to general practitioners that parents requesting surgery for their child's glue ear should be advised, where appropriate, of the likely effect of their own smoking upon the course of this disease. This will be increasingly important if tympanometric screening in schools becomes more widespread. A randomized controlled trial of anti-smoking advice prior to referral for glue ear surgery would provide useful information and could point to a means of limiting the progress of the modern "epidemic" of surgical intervention for this disease.

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8. TABLES

Table 1

Within-subject variability of spirometric indices in 232 children, from duplicate measurements on the same occasion.

Spirometric index	Standard deviation of a single measurement: Arithmetic scale S.D.	Arithmetic scale C.V.(%)	Log (base 10) scale S.D.	Log (base 10) scale antilog S.D.
FVC (ml)	81.25	5.0	0.0207	1.049
FEV1 (ml)	60.28	4.3	0.0209	1.049
FEV0.5 (ml)	75.73	7.7	0.0437	1.106
FEV0.5-1 (ml)	54.38	12.7	0.0489	1.119
PEF (ml/s)	217.66	7.0	0.0344	1.082
FEF25-75% (ml/s)	181.99	10.5	0.0529	1.130
FEF75-85% (ml/s)	142.24	18.0	0.0868	1.221
FEF25% (ml/s)	237.94	8.9	0.0448	1.109
FEF50% (ml/s)	208.95	11.1	0.0590	1.145
FEF75% (ml/s)	130.43	13.5	0.0686	1.171

Table 2

Chance probability (%) of an "abnormal" result in comparisons of FEV1 and PEFR with a baseline reading at the same test session, by criterion of abnormality and number of comparisons.

Criterion of "abnormality"		Number of comparisons with baseline reading 1	2	3	4	6	10
Largest	>10%	6.02	11.69	17.01	22.01	31.12	46.28
reduction	>15%	0.83	1.66	2.47	3.28	4.88	8.01
in FEV1	>20%	0.05	0.10	0.15	0.20	0.30	0.50
Largest	>10%	17.33	31.65	43.49	53.28	68.07	85.08
reduction	>15%	7.32	14.11	20.40	26.23	36.64	53.26
in PEFR	>20%	2.31	4.56	6.77	8.92	13.08	20.83

Table 3

Within-subject variability of spirometric indices in 171 children, from duplicate measurements on different occasions.

Spirometric index	Standard deviation of a single measurement Arithmetic scale S.D.	C.V.(%)	% between-occasion variance due to "measurement error"
FVC (ml)	121.67	7.5	45
FEV1 (ml)	117.08	8.3	27
FEV0.5 (ml)	109.27	11.2	48
FEV0.5-1 (ml)	61.53	14.3	78
PEF (ml/s)	376.00	12.1	34
FEF25-75% (ml/s)	257.90	14.8	50
FEF75-85% (ml/s)	191.01	24.1	56
FEF25% (ml/s)	378.02	14.2	40
FEF50% (ml/s)	273.60	14.5	58
FEF75% (ml/s)	197.22	20.4	44

Table 4

Distribution and reliability of spirometric indices among 232 children and the proportion of measured variance attributable to various factors.

Spirometric index	Mean	S.D	Reliability coefficient	Percentage of measured variance explained by: Within-subject	Height	Sex	Other
FVC (ml)	1632	262	0.78	22	37	9	32
FEV1 (ml)	1407	237	0.76	24	31	4	41
FEV0.5 (ml)	978	204	0.71	29	21	2	48
FEV0.5-1 (ml)	430	106	0.66	34	13	5	48
PEF (ml/s)	3100	683	0.70	30	23	1	46
FEF25-75% (ml/s)	1739	448	0.67	33	7	0	60
FEF75-85% (ml/s)	792	281	0.51	49	2	0	49
FEF25% (ml/s)	2669	635	0.65	35	15	0	50
FEF50% (ml/s)	1887	480	0.68	32	8	1	59
FEF75% (ml/s)	965	317	0.61	39	4	0	57

Table 5

Multiple regression coefficients for the effect of past and recent lower respiratory disease upon baseline spirometric indices.

Spirometric index	No LRD (mean)	LRD in past	Chest colds	Recent wheeze
FVC (ml)	1614.8	+39.1 (1.46)	-14.4 (0.61)	-23.1 (1.13)
FEV1 (ml)	1469.8	-1.8 (0.08)	-25.8 (1.28)	-53.8 (3.06)**
FEV0.5 (ml)	1045.6	-11.1 (0.57)	-24.8 (1.44)	-42.9 (2.87)**
FEF25-75% (ml/s)	1950.6	-135.4 (2.51)**	-101.9 (2.15)*	-203.2 (4.95)***
FEF75-85% (ml/s)	931.7	-72.2 (1.94)	-25.0 (0.76)	-99.9 (3.53)***
PEFR (ml/s)	3323.8	-63.5 (0.88)	-80.7 (1.27)	-55.5 (1.01)
FEF25% (ml/s)	2905.5	-91.5 (1.31)	-120.5 (1.96)	-170.3 (3.19)**
FEF50% (ml/s)	2087.0	-161.9 (2.78)**	-128.4 (2.50)*	-214.6 (4.83)***
FEF75% (ml/s)	1112.3	-71.8 (1.79)	-27.9 (0.79)	-122.4 (3.99)***
Number of children	622	61	83	114

All coefficients adjusted for sex, height, time of day, outside temperature and relative humidity, recent symptoms and housing tenure. For definition of disease groups see text.

Parameters for each group show the difference from the mean value for children with no history of lower respiratory disease.

Numbers in parentheses are t statistics for each parameter (869 df).
Significance level: * $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

Table 6

Multiple regression coefficients for the effect of past and recent lower respiratory disease upon baseline spirometric indices (ratio measures expressed as a percentage).

Spirometric index	No LRD (mean)	LRD in past	Chest colds	Recent wheeze
FEV1 /FVC	91.35	-2.22 (2.54)*	-0.26 (0.34)	-2.15 (3.24)**
FEV0.5 /FVC	65.11	-2.10 (2.00)*	-0.27 (0.29)	-1.74 (2.17)*
FEF25-75% /FVC (/s)	122.32	-10.48 (2.98)**	-4.79 (1.55)	-11.40 (4.25)***
FEF75-85% /FVC (/s)	58.66	-5.18 (2.05)*	-0.29 (0.13)	-5.66 (2.94)**
PEFR /FVC (/s)	207.70	-8.88 (2.04)*	-1.71 (0.45)	-0.07 (0.02)
FEF25% /FVC (/s)	181.87	-9.77 (2.23)*	-5.67 (1.47)	-8.19 (2.46)*
FEF50% /FVC (/s)	130.72	-12.25 (3.30)***	-6.51 (1.99)*	-12.17 (4.30)***
FEF75% /FVC (/s)	69.90	-5.28 (1.96)*	-0.51 (0.22)	-7.01 (3.42)***
Number of children	622	61	83	114

See footnotes to Table 5

Table 7

Percentage distribution of exercise-induced bronchial lability by history of wheeze and diagnosis of asthma

	Exercise-induced reduction in FEV1						Tested on treatment	Total
	<0%	0-5%	5-10%	10-15%	15-20%	>20%		
Total	39.2 (343)	31.1 (272)	15.8 (138)	5.9 (52)	2.2 (19)	4.6 (40)	1.3 (11)	875
Symptoms								
No history of wheeze	40.9 (288)	33.5 (236)	15.3 (108)	6.1 (43)	1.9 (13)	2.3 (16)	0.0 (0)	704
Wheezed, but not past year	48.3 (28)	24.1 (14)	13.8 (8)	5.2 (3)	1.7 (1)	6.9 (4)	0.0 (0)	58
Past yr, but not past mth	31.1 (23)	23.0 (17)	18.9 (14)	6.8 (5)	4.1 (3)	12.2 (9)	4.1 (3)	74
Wheezed past month (Nov.)	10.3 (4)	12.8 (5)	20.5 (8)	2.6 (1)	5.1 (2)	28.2 (11)	20.5 (8)	39
Diagnosis								
No wheeze past year	41.5 (316)	32.8 (250)	15.2 (116)	6.0 (46)	1.8 (14)	2.6 (20)	0.0 (0)	762
Wheeze past yr, no asthma	40.0 (20)	28.0 (14)	12.0 (6)	2.0 (1)	2.0 (1)	16.0 (8)	0.0 (0)	50
Asthma in past year	12.7 (8)	14.3 (9)	23.8 (15)	7.9 (5)	6.3 (4)	17.5 (11)	17.5 (11)	63

Numbers of children in parentheses
(six children with incomplete questionnaire data excluded).

Table 8

Prevalence (%) of symptoms related to asthma by recent wheeze and exercise-induced bronchial lability.

	No wheeze in past year				Wheeze in past year~			
Exercise-induced reduction in FEV1:	<0%	0-10%	10-20%	>20%	<0%	0-10%	10-20%	>20%
Night cough								
Any night in past month	15.2 (48)	16.5 (60)	11.7 (7)	40.0 (8)	26.9 (7)	31.8 (14)	45.5 (5)	60.0 (12)
3 or more nights in past month	9.2 (29)	11.0 (40)	10.0 (6)	20.0 (4)	15.4 (4)	15.9 (7)	27.3 (3)	35.0 (7)
Daytime cough								
Any day in past month	17.5 (55)	19.3 (70)	13.3 (8)	35.0 (7)	34.6 (9)	43.2 (19)	54.5 (6)	60.0 (12)
3 or more days in past month	13.7 (43)	14.3 (52)	11.7 (7)	20.0 (4)	26.9 (7)	27.3 (12)	27.3 (3)	50.0 (10)
School absence								
Any due to chest trouble past month	3.5 (9)	5.8 (9)	3.3 (1)	10.0 (2)	30.8 (8)	18.2 (8)	36.4 (4)	30.0 (6)
Chesty colds								
Colds went to the chest in past year	14.0 (44)	8.3 (30)	8.3 (5)	15.0 (3)	53.8 (14)	48.8 (21)	81.8 (9)	75.0 (15)
Hayfever								
In past year	7.0 (22)	6.6 (24)	6.7 (4)	20.0 (4)	7.7 (2)	36.4 (16)	27.3 (3)	35.0 (7)
No. of children	315	363	60	20	26	44	11	20

Numbers of children in parentheses.

~ Excludes eleven children tested on oral bronchodilator treatment or inhaled steroid therapy.

Table 9

Percent prevalence of respiratory symptoms, diagnosed asthma, inhaler use and degrees of exercise-induced bronchospasm by parental social class

	Social class of head of household						X^2trend (1 df)
	I	II	IIIN	IIIM	IV/V	Unknown~	
Night cough (7+ nights past month)	0.9 (1)	1.5 (4)	3.6 (7)	10.3 (22)	8.7 (10)	10.8 (12)	22.4
Colds to the chest past year	13.6 (15)	13.7 (36)	13.4 (26)	17.8 (38)	26.3 (30)	25.5 (28)	7.88
Wheeze past month	4.5 (5)	4.2 (11)	4.1 (8)	4.2 (9)	5.3 (6)	6.3 (7)	0.05
Wheeze past year	11.8 (13)	11.9 (31)	10.8 (21)	12.6 (27)	14.0 (16)	15.3 (17)	0.31
Asthma diagnosed at any age	10.0 (11)	8.4 (22)	8.2 (16)	9.3 (20)	6.1 (7)	10.8 (12)	0.42
Inhaler therapy past year	5.5 (6)	6.9 (18)	5.7 (11)	5.6 (12)	3.5 (4)	4.5 (5)	0.82
Number of replies	110	261	194	214	114	111	
Number tested	98	229	175	182	106	91	
Tested on therapy	1.0 (1)	0.4 (1)	2.3 (4)	1.6 (3)	0.9 (1)	1.1 (1)	
Exercise-induced reduction in FEV1 >20%	6.1 (6)	4.4 (10)	2.9 (5)	5.5 (10)	4.7 (5)	4.4 (4)	0.53
Exercise-induced reduction in FEV1 10-20%	7.1 (7)	7.0 (16)	5.1 (9)	12.1 (22)	8.5 (9)	9.9 (9)	
Exercise-induced reduction in FEV1 0-10%	52.0 (51)	47.2 (108)	44.6 (78)	48.4 (88)	48.1 (51)	41.8 (38)	
Exercise-induced reduction in FEV1 Increase	33.7 (33)	41.0 (94)	45.1 (79)	32.4 (59)	37.7 (40)	42.9 (39)	

~ Head of household student, armed forces, or never employed. These children have been excluded from the 1 df X^2 tests for trend.

Table 10

Middle ear pressure and relative gradient in 1721 tympanograms

M.E.P. (daPa)	Relative gradient (%) 0-	10-	20-	30-	40-	50-	60+	Total	(%)
Effusion~	108	0	0	0	0	0	0	108	(6.3)
-300 -	0	4	3	26	18	21	11	83	(4.8)
-250 -	0	0	10	12	21	10	2	55	(3.2)
-200 -	0	1	7	28	17	22	5	80	(4.7)
-150 -	0	3	16	43	54	31	17	164	(9.5)
-100 -	0	2	19	61	76	90	38	286	(16.6)
-50 - 0	0	2	37	171	262	183	52	707	(41.1)
Positive	0	0	8	67	66	68	29	238	(13.8)
Total (%)	108 (6.3)	12 (0.7)	100 (5.8)	408 (23.7)	514 (29.9)	425 (24.7)	154 (7.5)	1721	

Figures are number of tympanograms

~ Middle ear effusion, defined as zero relative gradient with tympanographic evidence of negative middle ear pressure (i.e. Type B tympanogram)

Table 11

Middle ear pressure and compliance in 1721 tympanograms

M.E.P. (daPa)	Compliance (ml) 0-	0.2-	0.4-	0.6-	0.8-	1.0-	1.2+	Total	(%)
Effusion~	78	30	0	0	0	0	0	108	(6.3)
-300 -	0	33	31	12	1	2	4	83	(4.8)
-250 -	0	8	19	11	10	4	3	55	(3.2)
-200 -	0	7	33	13	13	7	7	80	(4.7)
-150 -	0	28	64	28	19	11	14	164	(9.5)
-100 -	0	22	113	68	32	26	25	286	(16.6)
-50 - 0	0	65	286	205	85	34	32	707	(41.1)
Positive	0	31	83	65	28	15	16	238	(13.8)
Total	78	224	629	402	188	99	101	1721	
(%)	(4.5)	(13.0)	(36.6)	(23.4)	(10.9)	(5.8)	(5.9)		

Figures are number of tympanograms

~ Middle ear effusion, defined as zero relative gradient with tympanographic evidence of negative middle ear pressure (i.e. Type B tympanogram)

Table 12

Compliance and relative gradient in 1721 tympanograms

Compliance (ml)	Relative gradient (%) 0-	10-	20-	30-	40-	50-	60+	Total	(%)
0 -	78	0	0	0	0	0	0	78	(4.5)
0.2 -	30	5	31	83	36	28	11	224	(13.0)
0.4 -	0	6	57	230	202	120	14	629	(36.6)
0.6 -	0	1	7	75	188	116	15	402	(23.4)
0.8 -	0	0	3	11	67	84	23	188	(10.9)
1.0 -	0	0	1	3	13	51	31	99	(5.8)
1.2 +	0	0	1	6	8	26	60	101	(5.9)
Total	108	12	100	408	514	425	154	1721	
(%)	(6.3)	(0.7)	(5.8)	(23.7)	(29.9)	(24.7)	(7.5)		

Figures are number of tympanograms

Table 13

Relationship between middle ear pressure in each ear of the same child

Left M.E.P. (daPa)	Right M.E.P. (daPa) Effusion	-300 -	-200 -	-100-0	Positive	Total
Effusion	26	10	7	9	1	53
-300 -	8	25	23	13	3	72
-200 -	9	14	42	41	4	110
-100 - 0	9	14	53	371	53	500
Positive	3	2	4	47	58	114
Total	55	65	129	481	119	849

Figures are numbers of children

Table 14

Percentage distribution of middle ear pressure and effusion by selected respiratory symptoms.

M.E.P. (daPa)	Symptoms in week before tympanometry		Ear pain or discharge in past year		Tonsils or adenoids removed	
	Yes	No	Yes	No	Yes	No
-100 to +100	54.2 (216)	69.6 (329)	52.2 (108)	66.0 (419)	49.0 (51)	64.3 (475)
-200 to -100	19.9 (79)	14.8 (70)	18.4 (38)	16.7 (106)	13.5 (14)	17.6 (130)
-300 to -200	14.3 (57)	8.0 (38)	14.5 (30)	9.9 (63)	15.4 (16)	10.6 (78)
Effusion (no peak)	11.6 (46)	7.6 (36)	15.0 (31)	7.4 (47)	22.1 (23)	7.6 (56)
X^2 trend (1 df)	18.7		17.6		21.9	

Figures in parentheses are numbers of children

Table 15

Prevalence (%) of "lower" respiratory symptoms by home environment.

		Wheeze (past year)		Chesty colds (past year)		Night cough (3+ nights in past month)		Day cough (3+ days in past month)	
Tenure	own	10.7	(75/702)	13.5	(93/690)	7.8	(54/692)	13.2	(91/689)
	rent	*16.3	(49/301)	***27.4	(80/292)	***22.5	(66/293)	***22.0	(63/286)
Persons per room	<1.0	11.5	(39/338)	15.6	(52/334)	8.0	(27/336)	13.4	(45/335)
	1-1.5	13.3	(66/496)	17.2	(84/487)	*13.0	(63/486)	17.1	(83/484)
	1.5+	11.1	(14/126)	*25.0	(31/124)	**18.7	(23/123)	15.4	(18/117)
Smokers in household	0	12.1	(64/530)	14.8	(77/519)	9.0	(47/523)	13.9	(72/519)
	1	12.1	(37/307)	18.4	(55/299)	*14.0	(42/301)	16.5	(49/297)
	2+	13.4	(22/164)	**25.3	(41/162)	***19.5	(31/159)	20.4	(32/157)
Gas cooker	no	13.0	(55/422)	21.0	(87/414)	13.5	(56/415)	15.3	(63/411)
	yes	11.7	(68/579)	*15.2	(86/566)	11.2	(64/569)	16.0	(90/563)
Bottled gas stove	no	12.4	(114/920)	16.8	(151/901)	11.9	(108/905)	15.8	(141/895)
	yes	12.8	(10/78)	*27.6	(21/76)	13.2	(10/76)	14.3	(11/77)
Paraffin heater	no	12.4	(121/974)	17.6	(168/953)	11.8	(113/958)	15.6	(148/949)
	yes	12.5	(3/24)	16.7	(4/24)	21.7	(5/23)	17.4	(4/23)
Coal fire	no	12.5	(117/937)	17.5	(161/918)	11.7	(108/921)	15.2	(139/912)
	yes	11.5	(7/61)	18.7	(11/59)	21.7	(5/23)	17.4	(4/23)
Damp	none	10.6	(90/853)	15.3	(128/839)	10.7	(90/841)	14.7	(123/834)
other room		**20.9	(18/86)	*25.6	(21/82)	11.1	(9/81)	18.5	(15/81)
child's bedroom		**24.6	(15/61)	***37.3	(22/59)	***31.1	(19/61)	*25.9	(15/58)
Mould	none	10.5	(96/911)	15.6	(140/895)	11.7	(105/896)	15.3	(136/889)
other room		*23.4	(11/47)	**32.6	(15/46)	12.8	(6/47)	17.0	(8/47)
child's bedroom		***38.1	(16/42)	***43.6	(17/39)	21.4	(9/42)	26.3	(10/38)

Number of children in parentheses.

Significance of difference from prevalence in uppermost category:

* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

Table 16

Prevalence (%) of "upper" respiratory symptoms by home environment.

		Running nose (7+ days in past month)	Hayfever (past year)	Ear trouble (past year)	Sore throat (past year)
Tenure	own	12.5 (85/682)	10.8 (74/684)	24.1 (165/685)	50.4 (348/691)
	rent	*19.0 (54/284)	8.5 (24/281)	24.3 (70/288)	56.3 (166/295)
Persons per room	<1.0	12.4 (41/331)	9.6 (32/332)	26.3 (88/334)	51.2 (172/336)
	1-1.5	16.1 (77/477)	10.5 (50/478)	22.1 (106/480)	51.9 (252/486)
	1.5+	13.6 (16/118)	10.8 (13/120)	23.0 (28/122)	54.4 (68/125)
Smokers in household	0	10.9 (56/513)	10.2 (53/518)	23.5 (122/519)	51.1 (268/524)
	1	*17.2 (51/297)	10.3 (30/290)	25.3 (75/296)	52.5 (158/301)
	2+	**20.1 (31/154)	9.7 (15/155)	24.4 (38/156)	55.3 (88/159)
Gas cooking	no	14.7 (59/402)	10.6 (43/405)	21.9 (89/407)	53.1 (220/414)
	yes	14.2 (80/564)	9.7 (54/558)	25.9 (146/564)	51.4 (293/570)
Bottled gas stove	no	14.5 (129/887)	10.2 (91/889)	24.0 (214/892)	51.7 (467/904)
	yes	10.8 (8/74)	9.7 (7/72)	23.7 (18/76)	55.8 (43/77)
Paraffin heater	no	14.0 (131/939)	10.4 (97/937)	24.1 (228/945)	52.0 (498/958)
	yes	27.3 (6/22)	4.2 (1/24)	17.4 (4/23)	52.2 (12/23)
Coal fire	no	13.7 (124/904)	10.4 (94/903)	23.7 (215/909)	51.6 (475/920)
	yes	22.8 (13/57)	6.9 (4/58)	28.8 (17/59)	57.4 (35/61)
Damp	none	13.8 (114/824)	9.7 (80/824)	23.8 (197/829)	50.8 (427/840)
other room		17.3 (14/81)	**14.3 (12/84)	32.1 (27/84)	60.0 (51/85)
child's bedroom		17.2 (10/58)	8.9 (5/56)	18.3 (11/60)	56.7 (34/60)
Mould	none	13.3 (117/878)	9.8 (86/882)	23.2 (206/888)	52.1 (468/899)
other room		23.4 (11/47)	20.0 (9/45)	35.6 (16/45)	46.7 (21/45)
child's bedroom		*26.3 (10/38)	7.9 (3/38)	30.8 (12/39)	55.0 (22/40)

Number of children in parentheses.

Significance of difference from prevalence in uppermost category:

* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

Table 17

Prevalence (%) of wheeze in past year by mould in the home and exercise-induced bronchial lability

		No mould		Mould (any room)		Total	
Tested on treatment		100.0	(8/8)	100.0	(3/3)	100.0	(11/11)
Reduction	> 20%	48.6	(17/35)	60.0	(3/5)	50.0	(20/40)
in FEV1	10-20%	11.1	(7/63)	44.4	(4/9)	15.3	(11/72)
after	0-10%	8.9	(34/383)	33.3	(10/30)	10.7	(44/413)
exercise	Increase	6.6	(20/303)	14.7	(5/34)	7.4	(25/337)
Total		10.9	(86/792)	30.9	(25/81)	12.7	(111/873)

Numbers of children in parentheses

Table 18

Mean adjusted temperature and relative humidity in child's bedroom by occupancy, heating, ventilation, dampness and mould growth.

		Number of homes	Adjusted temp (°C)	(t)	Adjusted R.H. (%)	(t)
Child shares	No	128	18.1		51.5	
bedroom	Yes	189	17.7	-1.5	53.8	1.0
Heat in	None	113	17.1)		53.4)	
bedroom	Night only	104	17.8)		54.5)	
during				3.8		-2.6
winter	Day only	41	18.6)		50.5)	
months	Day & night	59	18.7)		50.7)	
Window usually	No	277	17.9		53.0	
open at night	Yes	40	17.7	-0.7	52.1	-0.8
Condensation	No	90	18.5		51.5	
forms on window	Yes	227	17.5	-4.6	53.5	2.5
Condensation or	No	270	17.9		54.3	
damp on walls	Yes	37	17.2	-2.4	56.7	3.8
Patches of	No	289	17.9		52.5	
mould or fungus	Yes	28	17.4	-1.2	56.7	3.2

Student's t tests for difference between means have 315 df.

Table 19

Prevalence (%) of symptoms by quintiles of bedroom relative humidity (simultaneous estimation from the moisture content of 778 wood blocks)

Symptoms	Quintiles of moisture content (low) 1	2	3	4	(high) 5	X^2 for 5 v 1-4 (1 df)	X^2 for trend (1 df)
In past month							
Night cough (any)	18.8	21.5	14.5	16.9	24.1	2.6	0.4
Day cough (any)	21.5	26.4	18.1	21.6	23.7	0.2	0.0
Running nose (any)	37.5	38.2	33.3	38.6	33.3	0.6	0.5
In past year							
Wheeze	10.6	13.8	12.3	16.2	8.9	1.8	0.0
Colds to the chest	15.7	20.1	12.4	14.1	20.0	1.5	0.1
Sore throat	53.8	47.2	54.0	52.0	55.2	0.4	0.3
Ear pain/discharge	23.7	28.1	24.3	22.4	20.9	0.7	0.9
Hay fever	13.4	15.2	6.0	9.5	8.0	0.7	4.3
Number of children~	159	142	145	172	160		

~ Total number of blocks returned. Missing questionnaire data reduced the numbers available for analysis for each symptom (minimum 766)

Table 20

Mean adjusted temperature and relative humidity in bedrooms of children with and without respiratory symptoms

Symptom	Mean adjusted temp (°C)			Mean adjusted R.H.(%)		
	No symptoms	With symptoms	(t)	No symptoms	With symptoms	(t)
In past month						
Night cough (any)	17.94	17.51	-1.9	52.74	53.34	0.7
Day cough (any)	17.91	17.55	-1.5	52.65	53.65	1.2
Running nose (any)	17.72	18.02	1.4	53.30	52.11	-1.5
In past year						
Wheeze	17.88	17.51	-1.3	52.73	53.87	1.1
Colds to the chest	17.88	17.65	-0.9	53.00	52.53	-0.5
Sore throat	17.81	17.85	0.2	52.64	53.09	0.6
Ear pain/discharge	17.80	17.89	0.4	52.67	53.51	1.0
Hay fever	17.78	18.32	1.4	52.99	51.69	-0.9

Student's t tests for differences between means have 315 df.

Table 21

Proportion of the variance in baseline spirometry explained by biological characteristics, test conditions and the home environment.

Outcome	Percentage of measured variance explained by: Sex and height	Test conditions	Tenure, density, cooking and damp	Ten other factors~	Variance unexplained*
FVC	46.5	1.6	0.8	0.4	50.6
FEV1	46.4	1.9	0.8	0.2	50.7
FEV0.5	34.3	2.1	0.6	0.3	62.7
FEF25-75%	14.0	1.2	1.3	0.5	83.0
FEF75-85%	9.4	1.0	0.6	0.5	88.6
PEFR	22.0	3.4	0.4	0.5	73.8
FEF25%	16.9	2.5	0.4	0.6	79.6
FEF50%	13.6	1.1	1.4	0.4	83.4
FEF75%	10.6	1.0	0.6	0.8	87.1

~ The ten other housing factors considered are described in the text.

* Includes a component due to measurement error

Table 22

Multiple regression coefficients for the effect of selected housing conditions upon baseline spirometric indices.

Outcome	Mean	Tenure (rented v owned)	Density (persons per room)	Cooking (gas v other)	Damp walls (any room v none)	Smokers (number in home)
FVC (ml)	1614.5	-27.4 (1.60)	-51.1 (2.69)**	-9.3 (0.66)	+24.2 (1.22)	+1.8 (0.18)
FEV1 (ml)	1462.6	-30.9 (2.11)*	-29.1 (1.79)	-20.5 (1.71)	+6.5 (0.38)	-0.2 (0.03)
FEV0.5 (ml)	1038.6	-21.7 (1.74)	-13.5 (0.97)	-14.8 (1.44)	-11.9 (0.82)	+0.1 (0.15)
FEF25-75% (ml/s)	1910.8	-47.3 (1.36)	-12.2 (0.31)	-69.3 (2.43)*	-78.1 (1.93)	-7.0 (0.35)
FEF75-85% (ml/s)	914.1	-20.3 (0.85)	+16.4 (0.61)	-33.6 (1.70)	-25.5 (0.91)	-9.6 (0.69)
PEFR (ml/s)	3313.3	-65.5 (1.42)	-66.8 (1.30)	-28.0 (0.74)	+17.0 (0.32)	+21.0 (0.78)
FEF25% (ml/s)	2874.9	-47.3 (1.04)	-37.3 (0.74)	-51.5 (1.38)	-34.2 (0.65)	+8.8 (0.33)
FEF50% (ml/s)	2042.3	-63.4 (1.68)	-18.4 (0.44)	-66.9 (2.16)*	-94.0 (2.14)*	+3.3 (0.15)
FEF75% (ml/s)	1091.9	-26.5 (1.02)	+8.4 (0.29)	-35.7 (1.67)	-36.6 (1.21)	-18.2 (1.20)

All regression coefficients are adjusted for sex, height, time of day, outside temperature and relative humidity.

Numbers in parentheses are t statistics (823 df).
Significance level: * $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

Table 23

Multiple regression coefficients for the effect of selected housing conditions upon baseline spirometric ratios (expressed as a percentage)

Outcome	Mean	Tenure (rented v owned)	Density (persons per room)	Cooking (gas v other)	Damp walls (any room v none)	Smokers (number in home)
FEV1 /FVC	90.97	-0.32 (0.58)	+1.19 (1.92)	-0.66 (1.44)	-1.13 (1.73)	-0.08 (0.26)
FEV0.5 /FVC	64.77	-0.13 (0.20)	+1.37 (1.84)	-0.49 (0.90)	-1.98 (2.55)*	+0.03 (0.08)
FEF25-75% /FVC (/s)	119.90	-1.44 (0.64)	+3.21 (1.28)	-3.33 (1.80)	-6.99 (2.66)**	-0.34 (0.26)
FEF75-85% /FVC (/s)	57.63	-0.45 (0.28)	+2.98 (1.66)	-1.38 (1.04)	-2.41 (1.28)	-0.61 (0.65)
PEFR /FVC (/s)	207.25	+0.11 (0.04)	+1.88 (0.61)	-0.05 (0.02)	-3.12 (0.97)	+1.28 (0.79)
FEF25% /FVC (/s)	180.01	-0.14 (0.05)	+3.20 (1.02)	-1.89 (0.81)	-5.86 (1.78)	+0.69 (0.42)
FEF50% /FVC (/s)	127.97	-2.38 (1.00)	+3.22 (1.22)	-3.30 (1.69)	-8.14 (2.93)**	+0.30 (0.21)
FEF75% /FVC (/s)	68.67	-0.70 (0.41)	+2.83 (1.48)	-1.48 (1.05)	-3.30 (1.65)	-1.08 (1.08)
FEF75-85% /FEF25-75%	47.52	+0.33 (0.42)	+1.39 (1.56)	-0.27 (0.40)	+0.54 (0.58)	-0.51 (1.10)
FEF75% /FEF50%	53.58	+0.44 (0.49)	+1.19 (1.20)	-0.23 (0.31)	+0.63 (0.61)	-1.18 (2.27)*

See footnotes to Table 23

Table 24

Prevalence (%) of degrees of exercise-induced bronchospasm by housing

		Exercise-induced reduction in FEV1				Tested on treatment~
		Increase	0 - 10%	10 - 20%	> 20%	
Tenure	own	35.8 (220)	49.8 (306)	8.3 (51)	5.2 (32)	0.8 (5)
	rent	46.0 (121)	40.7 (107)	8.0 (21)	3.0 (8)	2.3 (6)
Persons per room	<1.0	38.0 (111)	45.6 (133)	9.3 (27)	6.2 (18)	1.0 (3)
	1.0+	38.1 (209)	48.7 (267)	7.8 (43)	4.0 (22)	1.3 (2)
Smokers in home	none	37.5 (172)	48.2 (221)	8.3 (38)	5.0 (23)	1.1 (5)
	any	40.7 (167)	45.5 (189)	8.2 (34)	4.1 (17)	1.5 (6)
Gas cooker	no	37.3 (140)	48.8 (183)	8.0 (30)	4.0 (15)	1.9 (7)
	yes	39.9 (199)	46.1 (230)	8.4 (42)	4.8 (24)	0.8 (4)
Bottled gas	no	39.8 (322)	46.7 (378)	7.8 (63)	4.6 (37)	1.2 (10)
	yes	30.0 (19)	51.6 (33)	12.5 (8)	4.7 (3)	1.6 (1)
Paraffin heater	no	39.1 (332)	46.9 (399)	8.0 (68)	4.7 (40)	1.3 (11)
	yes	37.5 (9)	50.0 (12)	12.5 (3)	0.0 (0)	0.0 (0)
Coal fire	no	39.5 (324)	46.6 (382)	8.1 (66)	4.5 (37)	1.3 (11)
	yes	31.5 (17)	53.7 (29)	9.3 (5)	5.6 (3)	0.0 (0)
Dampness on walls	no	38.5 (286)	48.5 (360)	7.6 (56)	4.6 (34)	0.8 (6)
	yes	40.2 (53)	40.2 (53)	12.1 (16)	3.8 (5)	3.8 (5)
Mould growth	no	38.3 (303)	48.4 (383)	8.0 (63)	4.4 (35)	1.0 (8)
	yes	42.7 (35)	36.6 (30)	11.0 (9)	6.1 (5)	3.7 (3)

Number of children in parentheses. ~ Inhaled steroids or oral therapy.

Table 25

Prevalence (%) of middle ear effusion and underpressure in the more abnormal ear by sex, socioeconomic status and housing conditions.

		More negative middle ear pressure (daPa)			
		+100 to -100 (Type A)	-200 to -100 (Type C1)	-300 to -200 (Type C2)	Negative no peak (Type B)
Sex	male	63.1 (275)	17.0 (74)	12.4 (54)	7.6 (33)
	female	62.2 (271)	17.2 (75)	9.4 (41)	11.2 (49)
Social class of head of the house -hold	I	63.9 (62)	16.5 (16)	12.4 (12)	7.2 (7)
	II	63.9 (145)	14.5 (33)	14.5 (33)	7.1 (16)
	IIIN	62.4 (108)	21.4 (37)	5.2 (9)	11.0 (19)
	IIIM	65.2 (118)	17.7 (32)	6.6 (12)	10.5 (19)
	IV/V	62.9 (66)	14.3 (15)	17.1 (18)	5.7 (6)
	unknown~	52.8 (47)	18.0 (16)	12.4 (11)	16.9 (15)
Tenure	own	64.6 (396)	16.3 (100)	10.6 (65)	8.5 (52)
	rent	57.8 (147)	18.5 (47)	11.8 (30)	11.8 (30)
Persons per room	<1.0	64.2 (187)	15.5 (45)	12.7 (37)	7.6 (22)
	1-1.5	62.0 (268)	19.0 (82)	8.6 (37)	10.4 (45)
	1.5+	59.8 (65)	13.9 (15)	14.8 (16)	11.1 (12)
Smokers in household	0	63.9 (292)	17.3 (79)	10.7 (49)	8.1 (37)
	1	63.3 (169)	16.5 (44)	10.9 (29)	9.4 (25)
	2+	56.4 (79)	17.1 (24)	12.1 (17)	14.3 (20)
Gas cooker	no	60.5 (221)	21.1 (77)	11.0 (40)	7.4 (27)
	yes	64.1 (320)	14.2 (71)	10.6 (53)	11.0 (55)
Bottled gas	no	62.8 (504)	16.8 (135)	11.0 (88)	9.4 (75)
	yes	62.9 (39)	17.7 (11)	8.1 (5)	11.3 (7)
Paraffin heater	no	62.9 (530)	17.1 (144)	10.7 (90)	9.3 (78)
	yes	59.1 (13)	9.1 (2)	13.6 (3)	18.2 (4)
Coal fire	no	63.1 (511)	16.9 (137)	10.6 (86)	9.4 (76)
	yes	59.3 (32)	16.7 (9)	13.0 (7)	11.1 (6)
Dampness on walls	no	62.9 (462)	17.7 (130)	10.8 (79)	8.6 (63)
	yes	60.0 (78)	13.8 (18)	12.3 (16)	13.8 (18)
Mould growth	no	62.7 (492)	17.4 (137)	11.0 (86)	8.9 (70)
	yes	62.0 (49)	13.9 (11)	11.4 (9)	12.7 (10)

(Number of children in parentheses)
~ Head of the household student, armed forces or never employed.

Table 26

Mean adjusted weekly mean bedroom temperature and relative humidity by tympanogram type.

	Tympanogram types				F statistics~	
	A	C1	C2	B	ANOVA	trend
As measured						
Temperature (°C)	17.87	17.27	17.72	18.18	2.09	0.07
Relative humidity (%)	52.70	54.99	51.93	51.99	2.18	0.23
Adjusted for tenure and number of smokers						
Temperature (°C)	17.88	17.32	17.76	18.19	1.95	0.20
Relative humidity (%)	52.73	54.95	51.90	51.84	2.19	0.25
Number of children	190	50	33	34		

~ Tests for heterogeneity (ANOVA) have 3 and 303 df. All are $p > 0.05$. Tests for trend have 1 and 305 df. All are $p > 0.10$

Table 27

Frequency distribution of salivary cotinine concentrations by number of smokers in the household.

Number of smokers in the household	Quintiles of salivary cotinine (ng/ml) N.D.~	0.1-	0.4-	1.3-	3.6+	Total
0	111	160	93	30	11	405
1	1	22	58	87	73	241
2+	0	0	12	41	71	124
Total	112	182	163	158	155	770

~ Cotinine not detected (<0.1 ng/ml)

Table 28

Geometric mean salivary cotinine (ng/ml)~ by sex, housing tenure and number of smokers in the household

Tenure	Sex	Number of smokers in the household: None	One	Two or more
Owned	Male	0.15 (176)	0.99 (67)	2.75 (28)
	Female	0.18 (161)	1.15 (74)	3.00 (33)
Rented	Male	0.53 (35)	3.00 (53)	3.78 (30)
	Female	1.52 (33)	4.57 (47)	6.05 (33)

(Number of children in parentheses)
~ Undetectable levels recoded as 0.05ng/ml

Table 29

Adjusted~ odds ratio estimates for respiratory symptoms by quintiles of salivary cotinine and per doubling of cotinine concentration.

	Quintiles of salivary cotinine (ng/ml)					per doubling		
	N.D.	0.1-	0.4-	1.3-	3.6+	odds ratio	95% C.I.	X^2 (1df)
In past month								
Runny nose (7+ days)	1.0 (17)	0.53 (16)	0.67 (18)	1.11 (29)	0.95 (27)	1.05	0.95 -1.16	1.0
Night cough (3+ days)	1.0 (12)	0.76 (16)	0.53 (11)	1.23 (27)	0.93 (27)	1.04	0.93 -1.16	0.6
Daytime cough (3+ days)	1.0 (20)	0.55 (21)	0.56 (19)	1.00 (34)	0.56 (25)	1.00	0.95 -1.05	0.0
In past year								
Wheeze	1.0 (14)	0.93 (22)	0.81 (18)	1.33 (30)	0.55 (16)	0.97	0.88 -1.07	0.4
Chesty colds	1.0 (13)	0.91 (20)	1.34 (26)	1.73 (35)	2.04 (45)	1.14	1.04 -1.25	7.9**
Sore throat	1.0 (62)	0.74 (89)	0.92 (89)	0.91 (87)	0.68 (79)	0.97	0.90 -1.04	0.9
Ear trouble	1.0 (37)	0.41 (31)	0.65 (40)	0.68 (40)	0.73 (42)	0.99	0.92 -1.07	0.1
Hay fever	1.0 (16)	0.58 (16)	0.58 (14)	0.83 (18)	0.48 (10)	0.95	0.85 -1.07	0.7
Numbers tested	112	182	163	158	155			

(Numbers of affected children in parentheses).
~ All values adjusted for sex and housing tenure.
Significance of the log cotinine coefficient: ** $p < 0.01$

Table 30

Adjusted~ means for baseline spirometric indices by quintiles of salivary cotinine, and multiple regression coefficient per doubling of cotinine concentration.

	Quintiles of salivary cotinine (ng/ml)					per doubling		
	N.D.	0.1-	0.4-	1.3-	3.6+	coeff.	S.E.	t (750df)
FVC (ml)	1587	1648	1628	1613	1609	0.0	3.5	0.0
FEV1 (ml)	1459	1501	1470	1453	1451	- 3.7	3.0	-1.2
FEV0.5 (ml)	1042	1069	1045	1031	1033	- 3.5	2.6	-1.3
FEF25-75 (ml/s)	1951	1982	1926	1881	1862	-13.6	7.3	-1.9
FEF75-85 (ml/s)	968	946	884	902	895	-10.1	4.9	-2.1*
PEF (ml/s)	3185	3334	3234	3228	3209	- 5.9	9.8	-0.6
FEF25 (ml/s)	2880	2983	2888	2838	2858	-13.1	9.4	-1.4
FEF50 (ml/s)	2066	2116	2069	2008	1985	-11.9	7.9	-1.5
FEF75 (ml/s)	1143	1143	1076	1067	1066	-12.3	5.4	-2.3*
FEV1/FVC%	92.2	91.4	90.5	90.4	90.8	-0.21	0.12	-1.9
FEF25-75/FVC%	123.8	121.8	120.7	118.1	117.9	-0.74	0.47	-1.6
FEF75-85/FVC%	62.0	58.2	55.1	56.9	57.2	-0.59	0.33	-1.8
Number tested	111	179	162	152	153			

~ All values adjusted for sex, height, test conditions and housing tenure.
Significance of the log cotinine coefficient: * $p < 0.05$

Table 31

Percentage distribution of exercise-induced bronchospasm by quintiles of salivary cotinine.

Exercise-induced reduction in FEV1	Quintiles of salivary cotinine (ng/ml) N.D.	0.1-	0.4-	1.3-	3.6+
> 20%	2.7 (3)	5.1 (9)	3.7 (6)	7.3 (11)	4.6 (7)
10-20%	9.0 (10)	6.7 (12)	6.8 (11)	11.9 (18)	7.2 (11)
0-10%	46.9 (52)	51.1 (91)	50.0 (81)	43.7 (66)	44.4 (68)
Increase	41.4 (46)	37.1 (66)	39.5 (64)	37.1 (56)	43.8 (67)
Numbers tested (=100%)	111	178	162	151	153

(Numbers of children in parentheses)

Table 32

Prevalence (%) of tympanometric abnormalities in the the more abnormal ear by quintiles of salivary cotinine.

		More negative middle ear pressure (daPa)				
		+100 to -100 (Type A)	-200 to -100 (Type C1)	-300 to -200 (Type C2)	Negative no peak (Type B)	X^2 (trend) (1df)
Quintiles	N.D.	64.8 (70)	15.7 (17)	12.0 (13)	7.4 (8)	
of	0.1-	72.6 (130)	13.4 (24)	8.9 (16)	5.0 (9)	
salivary	0.4-	65.4 (104)	20.8 (33)	5.7 (9)	8.2 (13)	7.01**
cotinine	1.3-	61.0 (89)	17.8 (26)	6.9 (10)	14.4 (21)	
(ng/ml)	3.5+	58.3 (84)	16.7 (24)	12.5 (18)	12.5 (18)	

(Number of children in parentheses)
Significance level: * $p < 0.05$ ** $p < 0.01$

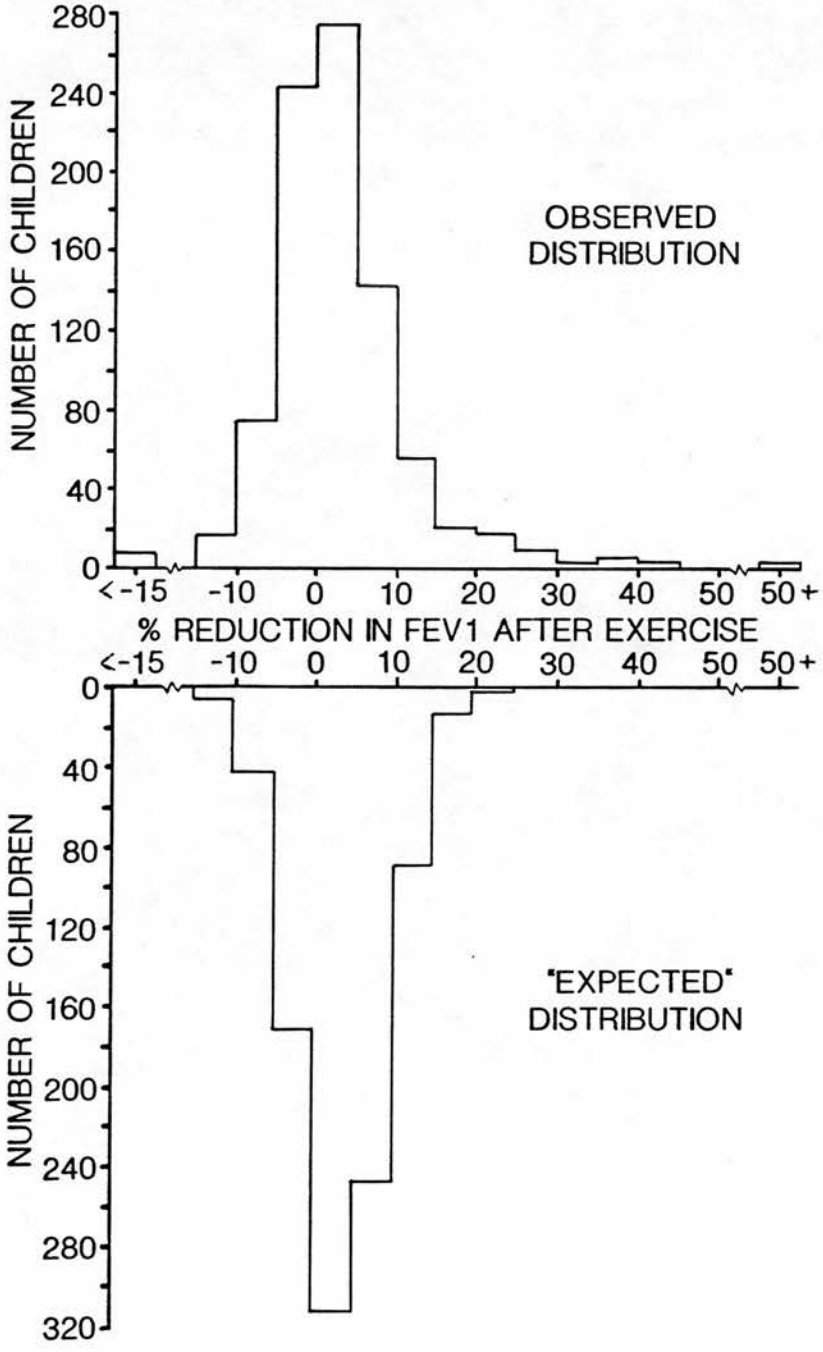
9. FIGURES

Figure 1

Frequency distribution of exercise-induced reduction in FEV1, and the distribution expected by chance alone

Data for Figure 1

% reduction in FEV1	Observed number	Expected number
< -15	8	0
-15 to -10	17	6
-10 to -5	75	43
-5 to zero	244	171
zero to 5	276	310
5 to 10	143	248
10 to 15	56	89
15 to 20	20	13
20 to 25	18	1
25 to 30	9	0
30 to 35	3	0
35 to 40	5	0
40 to 45	3	0
45 to 50	1	0
> 50	3	0


NUMBER OF CHILDREN
280
240
200
160
120
80
40
0
OBSERVED
DISTRIBUTION
<-15
-10
0
10
20
30
40
50
50+
% REDUCTION IN FEV1 AFTER EXERCISE
<-15
-10
0
10
20
30
40
50
50+
0
40
80
120
160
200
240
280
320
NUMBER OF CHILDREN
"EXPECTED"
DISTRIBUTION

10. APPENDICES

Appendix A Questionnaire sent to parents in November 1986

Telephone: 031–667 1011
Ext: 2344

Department of Community Medicine
Medical School
Teviot Place
Edinburgh EH8 9AG

CHEST TROUBLES AND HOUSING

Dear Parent or Guardian

Coughs, colds and chest troubles cause a lot of misery among young children and much worry for their parents. In this department we are carrying out a survey of children in their third school year throughout Edinburgh, to find out how housing conditions may affect children's health. The study is being carried out with the agreement of the headteacher, the Department of Education and the School Medical Service.

This letter is being sent to every parent with a child in the P3 year, so your family has not been chosen for any special reason. With this letter you will find a two-page questionnaire and a third sheet explaining further studies which we think will be helpful. In order to obtain useful results, it is important that everybody replies to the questionnaire. Personal information that we obtain will, of course, be treated as strictly confidential.

To avoid us having to contact you again, we would be very grateful if you would complete the questionnaire as soon as possible. Please return it to school in the same envelope in which you received it. We shall collect the envelopes unopened from a box in the classroom. We would appreciate your reply tomorrow, but, if this is not possible, we shall be pleased to accept replies through the school until 9.30am on Friday 28th November. Alternatively, if you wish, you can post the envelope to this Freepost address (no stamp required):

Dr D P Strachan
Department of Community Medicine
Freepost
Edinburgh
EH8 0LN

If you have any queries regarding this letter or the questionnaire, please do not telephone the school. I can be contacted between 4pm and midnight throughout this week on 031 332 4293 and I shall be pleased to help with any enquiries.

Thank you for helping us with our research into these important problems.

Yours sincerely

David Strachan

Dr. David Strachan

YOUR CHILD

Please do not write in this column

The questions on this sheet refer to the child who was given this questionnaire in school. Several questions are about wheezing. By this we mean breathing that makes a high-pitched whistling sound. Please tick the appropriate box in answer to each question.

1 During the past month, (since the school returned after the half-term holiday) has your child been:

a) absent from school due to chest trouble? Yes ☐ No ☐
If yes, for how many days in the month? _____

b) kept awake at night by coughing? Yes ☐ No ☐
If yes, for how many nights in the month? _____

c) troubled by cough during the daytime? Yes ☐ No ☐
If yes, for how many days in the month? _____

d) troubled by attacks of wheezing? Yes ☐ No ☐
If yes, for how many days in the month? _____

e) troubled by a blocked or runny nose? Yes ☐ No ☐
If yes, for how many days in the month? _____

2 During the past year, has your child suffered from:

a) one or more attacks of wheezing? Yes ☐ No ☐
b) undue breathlessness or wheezing after exercise? Yes ☐ No ☐
c) a tendency for colds to go to the chest? Yes ☐ No ☐
d) a sore throat? Yes ☐ No ☐
e) pain, discharge or infection in the ear? Yes ☐ No ☐
f) hay fever or frequent sneezing attacks? Yes ☐ No ☐

3 At any age, has your child suffered from:

a) wheezing? Yes ☐ No ☐
b) asthma? Yes ☐ No ☐
c) bronchitis? Yes ☐ No ☐
d) pneumonia? Yes ☐ No ☐

4 Has your child ever been admitted to hospital:

a) with wheezing or breathlessness? Yes ☐ No ☐
b) with some other chest trouble? Yes ☐ No ☐
c) for removal of tonsils or adenoids? Yes ☐ No ☐

If yes, please write the name of the hospital and the age at which your child was admitted on the back of this sheet.

5 Does your child take any medicines or inhalers regularly? Yes ☐ No ☐
If yes, please list them on the back of this sheet.

6 If you wish to make any other comments about your child's health, please do so on the back of this sheet.

PLEASE TURN OVER

YOUR HOUSE

Please do not write in this column

In these questions "your house" refers to the home where the child who was given this questionnaire usually lives.

1 How long has your child lived in this house? _____ years _____ months — 23

2 How many rooms are there in your house? (Not counting kitchens, bathrooms and toilets) _____ rooms — 24

3 How many adults (aged 16 or older) usually live in your house? _____ — 25

4 Including your child, how many children under 16 usually live in your house? _____ — 26

5 How many people in your household smoke cigarettes? _____ — 27

6 Which fuel(s) do you use for cooking? (tick more than one box if necessary) Electricity ☐ Gas ☐ Other ☐ — 28

7 Which fuel(s) do you use for heating? (tick more than one box if necessary) Electricity ☐ Coal ☐ Paraffin ☐ Wood ☐ Mains gas ☐ Oil ☐ Bottled gas ☐ Other ☐ — 29 30 31

8 In your child's bedroom, during the winter months:

a) does your child share the room with others?	Yes ☐ No ☐	32
b) is the room usually heated during the day?	Yes ☐ No ☐	33
c) is the room usually heated at night?	Yes ☐ No ☐	34
d) is the window usually left open at night?	Yes ☐ No ☐	35
e) does condensation ever form on the window?	Yes ☐ No ☐	36
f) does condensation ever form on the walls?	Yes ☐ No ☐	37
g) are there any patches of mould or fungus?	Yes ☐ No ☐	38

9 Please list any other rooms in your house that are affected by:

a) condensation on the window: — 39

b) condensation or dampness on the walls: — 40

c) patches of mould or fungus: — 41

10 Is your house: (tick one box only)
- rented from the local authority (council)? ☐
- rented from a private landlord? ☐
- rented from a housing association? ☐
- owned or bought on a mortgage? ☐

— 42

11 Please describe the occupation of the main wage-earner in your household. If the main wage-earner is unemployed, tick this box ☐ and state the nature of his or her last occupation: — 43 44 45 46

12 If you would like to add any comments about your housing, please do so on the back of this sheet. — 47 48 49 50

PLEASE TURN OVER

Thank you for completing the questionnaire.

We hope to find out more about the links between housing conditions and children's health by performing some simple tests at school on about one thousand primary school children. We shall also be measuring the humidity of the air in the homes of some of the children. We hope that you will agree to your child taking part in these further studies.

The tests that we think will be helpful are:

1 Measurement of height.
2 Breathing tests to see how fast your child can blow air out of the lungs.
3 A similar breathing test after your child has been running at his or her own speed for six minutes.
4 A test for "glue ear" (fluid in the middle ear) which involves wearing an earphone on each ear for half a minute while the pressure in the ear canal is gently varied up and down (like going up and down in a lift).

These tests have been widely used in young children and do not result in any discomfort or danger for the child. Indeed, we expect that most children will find them enjoyable. I have trained as a general practitioner (family doctor) and I shall be present at all the tests. If your child is suffering from chest trouble, they may point to possible causes, but even if your child appears to be healthy, they may show up something which requires further investigation. If this occurs, you will be informed. Only with your permission would we tell the school doctor and your child's family doctor.

It may also be helpful for us to look at your child's medical records kept by your family doctor, the school doctors and in hospital, and to find out how often your child has been absent from school. Such information would be treated as strictly confidential.

We would be very grateful if you could help us with our further studies by giving your consent below.

I have read the explanation above and I agree that:

a) My child may be tested as described. Yes ☐ No ☐

b) My child's medical records may be examined. Yes ☐ No ☐

c) My child's school attendance records may be examined. Yes ☐ No ☐

Your name (capitals): Parent/Guardian

Your address: Telephone:

Child's name: Date of birth:

Name and address of your child's family doctor:

Signed: Date:

PLEASE RETURN THE QUESTIONNAIRE AND THIS SHEET TO THE SCHOOL TOMORROW

Thank you

Instructions for the wood block survey, January 1987

Telephone: 031–667 1011
Ext: 2344

University of Edinburgh

Department of Community Medicine
Medical School
Teviot Place
Edinburgh EH8 9AG

13 January 1987

CHEST TROUBLES AND HOUSING

Dear

Towards the end of last term you kindly replied to our questionnaire survey of housing and health in P3 children, and indicated that you were willing for your child to take part in further tests at school. While we are doing these medical tests, we are interested in measuring the humidity (dampness) of the air in each child's home. One simple way to do this in a large number of houses at the same time is to allow a small block of wood to absorb moisture from the air. We would be most grateful if you could help us to make such a measurement in your home over the next seven days. This involves nothing more than following these few simple instructions:

1. Please find the block of wood enclosed with this letter. Keep the padded "Jiffy" envelope and the resealable plastic bag inside it in a safe place.
2. This evening, place the block of wood in the bedroom of the child who is included in our survey, about 2 or 3 feet off the floor. If possible, place it at least 3 feet from the window and a similar distance away from any fires or radiators. On top of a bedside cabinet or chest of drawers would be suitable.
3. Leave the block there for one week. It can be moved for dusting etc. but otherwise please leave it undisturbed.
4. On the morning of Tuesday 20th January put the block in the resealable plastic bag provided. Press the seal together firmly so that it is airtight (check this by squeezing the bag gently to see if air can escape). Give it to your child in the padded envelope to return to the collection box in the classroom.
5. A letter will be circulated in class on Monday 19th January to remind you to return the block the next day.

We shall collect the wood blocks from school and measure their water content using an instrument similar to that used by surveyors in dampness surveys of buildings. This will indicate how humid the air has been in your child's bedroom over the past week, on average. This is a simple survey but will involve a large number of homes. We think that it will provide us with much useful information. Later, we shall be approaching a smaller number of families personally to ask if we can obtain more detailed measurements in their homes, using special instruments.

We hope you will feel that *you* can help us with these further studies. If you have any queries about this letter, please do not hesitate to telephone me on 031 332 4293 any time between 4pm and midnight this evening.

Thank you

Yours sincerely

David Strachan

(Dr) David Strachan

Appendix B Ventilatory Function Testing

American Thoracic Society Protocol

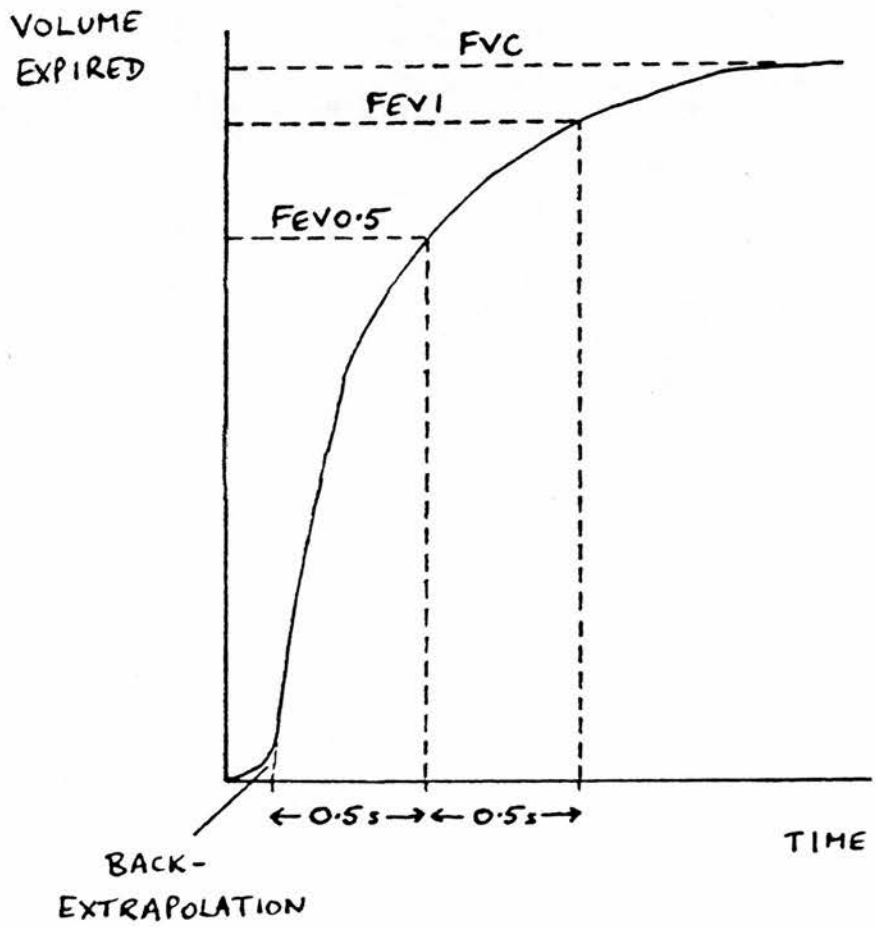
Subjects are instructed in the FVC manoeuvre and the appropriate techinique is demonstrated. A minimum of three acceptable manoeuvres are performed. Acceptability is determined by the technician's observations that the subject understood the instructions and performed the test with a smooth continuous exhalation, with apparent maximal effort, with a good start, and without coughing, glottis closure, early termination, air leak, obstruction of the mouthpiece, excessive hesitation or false starts. The two best of the acceptable curves should not vary by more than 5% of the reading or 100 ml, whichever is the greater. Nose clips are recommended but not required. In children under the age of 12, standing or sitting position should be indicated.

Spirometric variables should be measured from a series of at least three acceptable forced expiratory curves. The maximal FVC and the maximal FEV1 are recorded, even if these values do not come from the same curve. If flow rates are obtained from a single test, the test used should be the one with the greatest sum of FEV1 and FVC. Summing the FEV1 and FVC provides an objective and simple method of defining the "best" curve.

Glossary of Terms and Abbreviations (see diagram also)

FVC	Forced vital capacity
FEV1	Forced expiratory volume in one second
FEV0.5	Forced expiratory volume (first half second)
FEV0.5-1	Forced expiratory volume (second half second)
FEF25-75%	Forced expiratory flow from 25% to 75% of FVC
FEF75-85%	Forced expiratory flow from 75% to 85% of FVC
FEFn%	Flow rate when n% of FVC has been expired
PEFR	Peak expiratory flow rate
BTPS	Body temperature and pressure saturated with water vapour

Back-extrapolation allows for the initial period of submaximal flow in imputing a zero time for calculation of FEV1 and FEV0.5.



Appendix C Impedance Tympanometry

A soft rubber tip seals the tympanometer probe in the ear canal. The pinna is pulled downwards and outwards (in children) to straighten the ear canal. The pressure in the ear canal is automatically increased to +200 daPa (approx 200 mm water above atmospheric pressure) which tenses the tympanic membrane. The compliance (lack of resistance) of the air in the external ear as it vibrates in response to the continuous tone generated by the probe indicates the physical volume of the ear canal. Low physical volume (with a flat tympanogram) suggests blockage by wax. Values in excess of 2 ml in young children suggest tympanic perforation or a patent ventilation tube.

The pressure in the ear canal is then reduced through zero (atmospheric) to -312 daPa. The tympanic membrane becomes increasingly relaxed as pressure equalizes on either side of the drum. When external ear pressure equals middle ear pressure, the drum vibrates most freely in response to the probe tone, and the compliance of the ear is maximal. This tympanometric peak therefore defines middle ear pressure and the peak compliance indicates middle ear compliance, assuming zero compliance at +200 daPa. The relative gradient of the tympanogram is an expression of the steepness of

the peak. It is derived as the ratio of absolute gradient (ml per 50 daPa pressure change) to peak compliance (see diagram).

When fluid is present in the middle ear, the ossicles are unable to vibrate in response to the probe tone, despite flaccidity of the drum at highly negative external ear pressures. Thus the middle ear compliance is low and the peak is poorly defined. This is quantified by relative gradient less than 10% (Type B tympanogram).